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* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JUL 02	LMEDLINE coverage updated
NEWS	3	JUL 02	SCISEARCH enhanced with complete author names
NEWS	4	JUL 02	CHEMCATS accession numbers revised
NEWS	5	JUL 02	CA/CAPplus enhanced with utility model patents from China
NEWS	6	JUL 16	CAplus enhanced with French and German abstracts
NEWS	7	JUL 18	CA/CAPplus patent coverage enhanced
NEWS	8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	9	JUL 30	USGENE now available on STN
NEWS	10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	12	AUG 13	CA/CAPplus enhanced with additional kind codes for granted patents
NEWS	13	AUG 20	CA/CAPplus enhanced with CAS indexing in pre-1907 records
NEWS	14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	15	AUG 27	USPATOLD now available on STN
NEWS	16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	18	SEP 13	FORIS renamed to SOFIS
NEWS	19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	20	SEP 17	CA/CAPplus enhanced with printed CA page images from 1967-1998
NEWS	21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	23	OCT 02	CA/CAPplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	24	OCT 19	BEILSTEIN updated with new compounds
NEWS	25	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	26	NOV 19	WPIX enhanced with XML display format
NEWS EXPRESS	19	SEPTEMBER 2007:	CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 12:43:22 ON 27 NOV 2007

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 12:43:30 ON 27 NOV 2007

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 NOV 2007 HIGHEST RN 955995-34-3

DICTIONARY FILE UPDATES: 26 NOV 2007 HIGHEST RN 955995-34-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

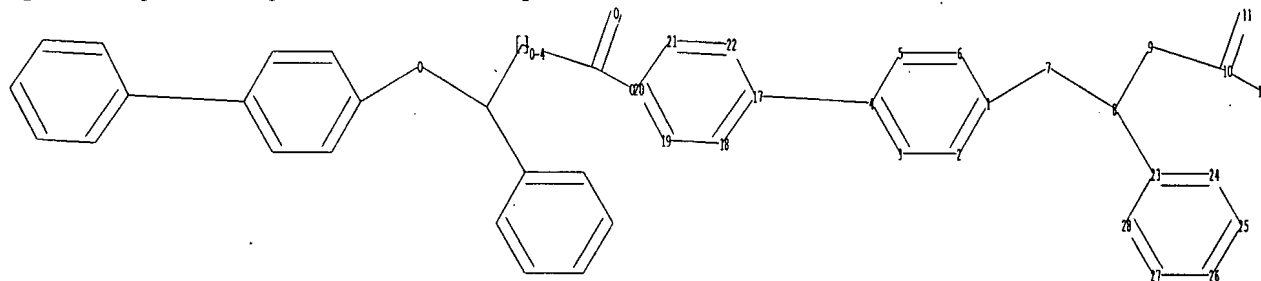
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10823842b.str



chain nodes :

7 8 9 10 11 14

ring nodes :

1 2 3 4 5 6 17 18 19 20 21 22 23 24 25 26 27 28

chain bonds :

1-7 4-17 7-8 8-9 8-23 9-10 10-11 10-14

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22 23-24
 23-28 24-25 25-26 26-27 27-28
 exact/norm bonds :
 1-7 7-8 10-11 10-14
 exact bonds :
 4-17 8-9 8-23 9-10
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22 23-24
 23-28 24-25 25-26 26-27 27-28
 isolated ring systems :
 containing 1 :

G1:C,O,S,N

Match level :

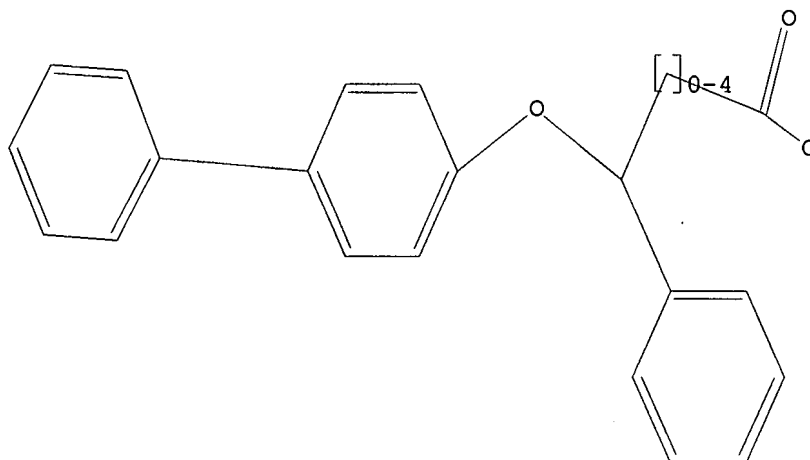
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 11:CLASS 14:CLASS 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom
 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 12:43:46 FILE 'REGISTRY'
 SAMPLE SCREEN SEARCH COMPLETED - 107 TO ITERATE

100.0% PROCESSED 107 ITERATIONS
 SEARCH TIME: 00.00.02

3 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
 PROJECTED ITERATIONS: 1520 TO 2760
 PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 12:43:52 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 2020 TO ITERATE

100.0% PROCESSED 2020 ITERATIONS

74 ANSWERS

SEARCH TIME: 00.00.01

L3 74 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

172.10

172.31

FILE 'CAPLUS' ENTERED AT 12:43:57 ON 27 NOV 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 27 Nov 2007 VOL 147 ISS 23

FILE LAST UPDATED: 26 Nov 2007 (20071126/ED)

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<http://www.cas.org/infopolicy.html>

=> s l3 full

L4 23 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:157200 CAPLUS

DOCUMENT NUMBER: 147:22680

TITLE: Discovery of new potent human protein tyrosine phosphatase inhibitors via pharmacophore and QSAR analysis followed by in silico screening

AUTHOR(S): Taha, Mutasem O.; Bustanji, Yasser; Al-Bakri, Amal G.; Yousef, Al-Motassem; Zalloum, Waleed A.; Al-Masri, Ihab M.; Atallah, Naji

CORPORATE SOURCE: Department of Pharmaceutical Sciences, Faculty of Pharmacy, University of Jordan, Amman, Jordan

SOURCE: Journal of Molecular Graphics & Modelling (2007), 25(6), 870-884

CODEN: JMGMMFI; ISSN: 1093-3263

PUBLISHER: Elsevier Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A pharmacophoric model was developed for human protein tyrosine phosphatase 1B (h-PTP 1B) inhibitors utilizing the HipHop-REFINE module of CATALYST software. Subsequently, genetic algorithm and multiple linear regression anal. were employed to select an optimal combination of physicochem. descriptors and pharmacophore hypothesis that yield consistent QSAR equation of good predictive potential ($r = 0.87$, $F\text{-statistic} = 69.13$, $r^2_{BS} = 0.76$, $r^2_{LOO} = 0.68$). The validity of the QSAR equation and the associated pharmacophoric hypothesis was exptl. established by the identification of five new h-PTP 1B inhibitors retrieved from the National Cancer Institute (NCI) database.

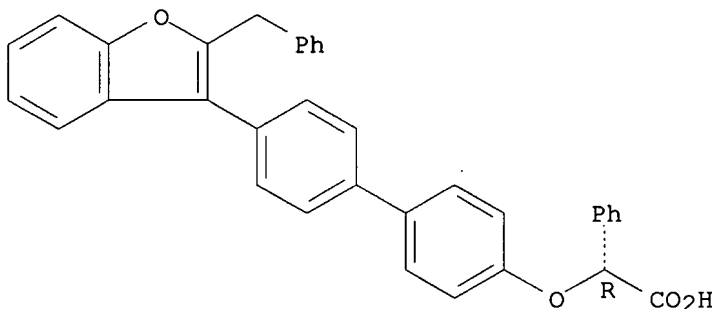
IT 250341-99-2 263759-84-8

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of new potent human protein tyrosine phosphatase inhibitors via pharmacophore and QSAR anal. followed by in silico screening)

RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

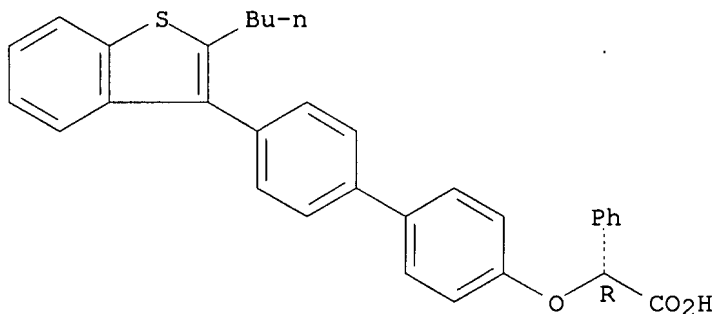
Absolute stereochemistry.



RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1208347 CAPLUS

DOCUMENT NUMBER: 144:31955

TITLE: Effects of Variable Docking Conditions and Scoring Functions on Corresponding Protein-Aligned Comparative Molecular Field Analysis Models Constructed from Diverse Human Protein Tyrosine Phosphatase 1B

Inhibitors
 AUTHOR(S): Taha, Mutasem O.; AlDamen, Murad A.
 CORPORATE SOURCE: Department of Pharmaceutical Sciences, Faculty of
 Pharmacy, University of Jordan, Amman, Jordan
 SOURCE: Journal of Medicinal Chemistry (2005), 48(25),
 8016-8034
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The effects of variable docking conditions and scoring functions on
 corresponding protein-aligned comparative mol. field anal. (CoMFA) models
 have been assessed. To this end, a group of diverse inhibitors were
 docked into the active site of human protein tyrosine phosphatase 1B
 (h-PTP 1B). The docked structures were utilized to construct
 corresponding protein-aligned CoMFA models by employing probe-based (H+,
 OH, CH3) energy grids and genetic partial least squares (G/PLS)
 statistical anal. A total of 48 different docking configurations were
 evaluated, of which some succeeded in producing self-consistent and
 predictive CoMFA models. However, the best CoMFA model coincided with
 docking the un-ionized ligands into the hydrated form of the binding site
 via the PLP1 scoring function and restricted docking settings ($r^2(\text{LOO}) =$
 0.647 , $r^2(\text{PRESS})$ against 27 test compds. $= 0.617$). Interestingly, the
 most significant CoMFA models were orthogonal and corresponded to
 significantly different docked conformers/poses. To utilize the
 predictive potentials of the best CoMFA models collectively, it was
 decided to combine them in a single quant. structure-activity relationship
 (QSAR) model. HThe combination model illustrated excellent statistical
 properties ($r^2(\text{LOO}) = 0.890$, $r^2(\text{PRESS})$ against 27 test compds. $= 0.750$).

IT 250341-99-2 263759-84-8

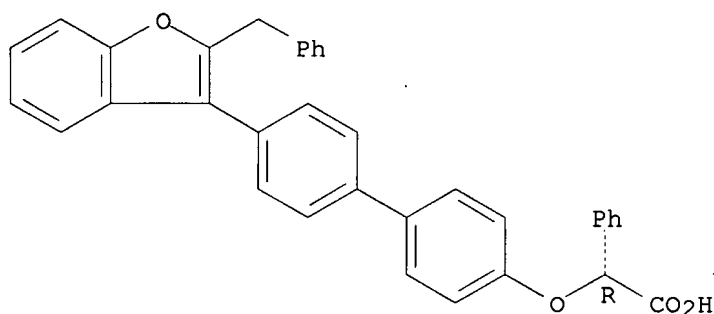
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(docking conditions and scoring functions effect on corresponding
 protein-aligned CoMFA models constructed from diverse protein tyrosine
 phosphatase 1B inhibitors)

RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-
 biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

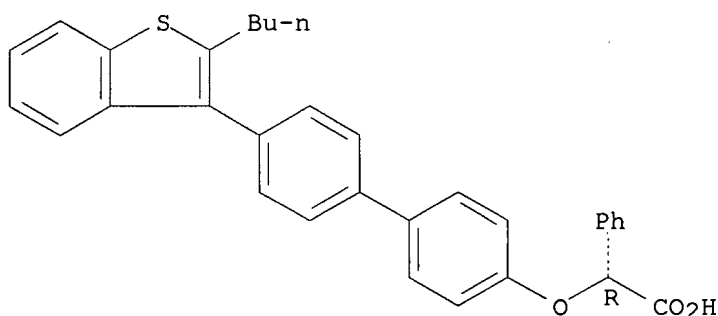
Absolute stereochemistry.



RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-
 biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:904352 CAPLUS

DOCUMENT NUMBER: 143:248386

TITLE: Preparation of substituted azole derivatives for treating diseases mediated by PTPase activity

INVENTOR(S): Mjalli, Adnan M. M.; Poliseti, Dharma R.; Subramanian, Govindan; Quada, James C.; Arimilli, Murty N.; Yarragunta, Ravindra R.; Andrews, Robert C.; Xie, Rongyuan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 204 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

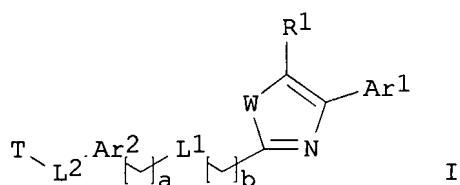
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187277	A1	20050825	US 2005-56498	20050211
AU 2005214349	A1	20050901	AU 2005-214349	20050211
CA 2551909	A1	20050901	CA 2005-2551909	20050211
WO 2005080346	A1	20050901	WO 2005-US4590	20050211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1730118	A1	20061213	EP 2005-723026	20050211
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1922151	A	20070228	CN 2005-80004860	20050211
JP 2007523903	T	20070823	JP 2006-553310	20050211
IN 2006KN02467	A	20070525	IN 2006-KN2467	20060829
PRIORITY APPLN. INFO.:			US 2004-543971P	P 20040212
			WO 2005-US4590	W 20050211

OTHER SOURCE(S): MARPAT 143:248386

GI



AB The title compds. I [a, b = 0-2; W = O, S, NR2 (wherein R2 = alkyl, etc.); R1 = H, halo, CN, etc.; L1 = a direct bond, (un)substituted NHCO, NHSO2, etc.; Ar1 = (un)substituted (hetero)aryl, fused cycloalkylaryl, etc.; Ar2 = (un)substituted (hetero)arylene, fused arylcycloalkylene, etc.; L2 = CH2, O, alkylene, etc.] which can be useful as inhibitors of protein tyrosine phosphatases and thus can be useful for the management, treatment, control, or the adjunct treatment of diseases mediated by PTPase activity such as type I diabetes and type II diabetes, were prepared. Thus, treating 4-(2,4-dichlorophenyl)-2-[2-(4-methoxyphenyl)-(E)-vinyl]-1H-imidazole with Me bromoacetate followed by ester hydrolysis afforded 56% {4-(2,4-dichlorophenyl)-2-[2-(4-methoxyphenyl)-(E)-vinyl]-1H-imidazol-1-yl}acetic acid. The representative compds. I were tested for inhibition of PTP-1B. In general, the exemplified compds. I may inhibit PTP-1B with IC50 of less than 20 μ M. The pharmaceutical compns. comprising the compds. I, and their use in treating human or animal disorders are also disclosed.

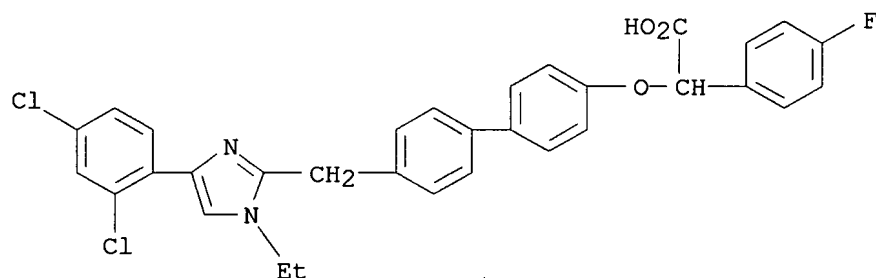
IT 863246-34-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted azole derivs. for treating diseases mediated by PTPase activity)

RN 863246-34-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-[[4-(2,4-dichlorophenyl)-1-ethyl-1H-imidazol-2-yl]methyl][1,1'-biphenyl]-4-yl]oxy]-4-fluoro- (CA INDEX NAME)



L4 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:996166 CAPLUS

DOCUMENT NUMBER: 141:424432

TITLE: Preparation of heterocycle substituted carboxylates, including amino acid derivatives, as inhibitors of protein tyrosine phosphatases for treatment of diabetes, cancer, and related conditions

INVENTOR(S): Whitehouse, Darren; Hu, Shaojing; Fang, Haiquan; Combs, Kerry; Van Zandt, Michael

PATENT ASSIGNEE(S): The Institute of Pharmaceutical Discovery, LLC, USA

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099192	A2	20041118	WO 2004-US13702	20040430
WO 2004099192	A3	20050113		
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CA 2523743	A1	20041118	CA 2004-2523743	20040430
US 2005004114	A1	20050106	US 2004-835818	20040430
EP 1628970	A2	20060301	EP 2004-751194	20040430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006525366	T	20061109	JP 2006-514245	20040430
MX 2005PA11539	A	20060123	MX 2005-PA11539	20051026
PRIORITY APPLN. INFO.:			US 2003-467214P	P 20030430
			WO 2004-US13702	W 20040430
OTHER SOURCE(S):		MARPAT 141:424432		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. I [wherein R1 = H, phenyl/alkyl, alkenyl; L = a bond, SO2, CO, O, S, SO, etc.; L2 = a bond, NH and derivs., O, S, SO2, SO, NHCO, etc.; L3 = a bond, alkylene, CO, etc.; R2 = H, halo, (un)substituted arylalkoxy, aryl, arylalkyl, etc.; R20, R21, R22, R23 = independently H, halo, alkyl, OH, alkoxy, NO2, NH2, (un)substituted arylalkoxy, arylalkyl, etc.; A = (un)substituted hetero/aryl; B = (un)substituted heterocycloalkyl, heteroaryl; Q = H, (un)substituted heterocycloalkyl, hetero/aryl, etc.; Y = a bond, (un)substituted -O-alkylene-; Z = absent or (un)substituted phenyl] and their pharmaceutically acceptable salts which are useful in the treatment of metabolic disorders related to insulin resistance, leptin resistance, or hyperglycemia (no data). Compds. of the invention include inhibitors of protein tyrosine phosphatases, in particular protein tyrosine phosphatase-1B (PTP-1B), that are useful in the treatment of diabetes and other PTP mediated diseases, such as cancer, neurodegenerative diseases, and the like (no data). Also disclosed are pharmaceutical compns. comprising compds. of the invention and methods of treating the aforementioned conditions using such compds. For example, II was prepared by Suzuki cross coupling of bromide III (preparation given) with [4-(dibenzofuran-4-yl)phenyl]boronic acid (preparation given), and Boc-deprotection. Preferred I exhibited IC50 ≤ 300 nM in an in vitro inhibitory activity test against recombinant human PTP1B with phosphotyrosyl dodecapeptide TRDI(P)YETD(P)Y(P)YRK.

IT 796033-45-9P, 2-[[4'-(10-(Ethoxycarbonyl)pyrido[1,2-a]indol-3-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid

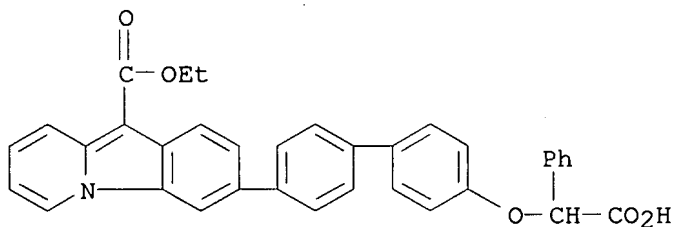
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(PTP-1B inhibitor; preparation of heterocycle substituted carboxylates,
including amino acid derivs., as PTP-1B inhibitors for treatment of
diabetes, cancer, and related conditions)

RN 796033-45-9 CAPLUS

CN Pyrido[1,2-a]indole-10-carboxylic acid, 3-[4'-(carboxyphenylmethoxy)[1,1'-
biphenyl]-4-yl]-, 10-ethyl ester (CA INDEX NAME)



L4 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:996147 CAPLUS

DOCUMENT NUMBER: 141:424429

TITLE: Preparation of substituted carboxylic acids, including
amino acid derivatives, as inhibitors of protein
tyrosine phosphatases for treatment of diabetes,
cancer, and related conditions

INVENTOR(S): Van Zandt, Michael C.; Whitehouse, Darren; Combs,
Kerry; Hu, Shaojing

PATENT ASSIGNEE(S): The Institutes for Pharmaceutical Discovery, LLC, USA

SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099168	A2	20041118	WO 2004-US11371	20040414
WO 2004099168	A3	20050224		
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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004236173	A1	20041118	AU 2004-236173	20040414
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US 2004266788	A1	20041230	US 2004-823842	20040414
EP 1620420	A2	20060201	EP 2004-760538	20040414
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
BR 2004009914	A	20060425	BR 2004-9914	20040414
CN 1812977	A	20060802	CN 2004-80018416	20040414
JP 2006525329	T	20061109	JP 2006-509981	20040414
NO 2005004957	A	20060123	NO 2005-4957	20051025

MX 2005PA11524	A	20060321	MX 2005-PA11524	20051026
IN 2005KN02124	A	20070608	IN 2005-KN2124	20051026
PRIORITY APPLN. INFO.:			US 2003-467057P	P 20030430
			WO 2004-US11371	W 20040414

OTHER SOURCE(S): MARPAT 141:424429
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. I [wherein X = (CH₂)_n; n = 0-4; R₁ = phenyl/alkyl, alkenyl; R₂ = Ph, phenyl/alkyl, alkyl-CONH₂, hydroxyalkyl, etc; R₂₀, R₂₁, R₂₂, R₂₃ = independently H, arylalkoxy, aryl/halo/alkyl, halo, OH and derivs., NO₂, NH₂, NH-aryl, wherein each of the above aryl groups are optionally substituted, etc.; L = SO₂NH, NHSO₂, SO₂, NH, O, CONH, CO-alkyl, etc.; L₃ = a bond, absent, CO, CONH, NHCO, etc.; A = (un)substituted aryl, selected from Ph, naphthyl, fluorenyl, or heteroaryl; Q = H, arylhetero/aryl/heteroarylalkyl/heteroaryl/hetero/aryl, wherein the aryl group = (un)substituted Ph, naphthyl, or fluorenyl] and their pharmaceutically acceptable salts which are useful in the treatment of metabolic disorders related to insulin resistance, or hyperglycemia (no data). Compds. of the invention include inhibitors of protein tyrosine phosphatases, in particular protein tyrosine phosphatase-1B (PTP-1B), that are useful in the treatment of diabetes and other PTP mediated diseases, such as cancer, neurodegenerative diseases, and the like (no data). Also disclosed are pharmaceutical compns. comprising compds. of the invention and methods of treating the aforementioned conditions using such compds. For example, II was prepared in 5 steps from 2,4'-dibromoacetophenone, ester II, and benzyl bromide. Preferred I exhibited IC₅₀ ≤ 300 nM in an in vitro inhibitory activity test against recombinant human PTP1B with phosphotyrosyl dodecapeptide TRDI(P)YETD(P)Y(P)YRK.

IT 796033-34-6P, 2-[[4'-[3-(Benzylamino)imidazo[1,2-a]pyridin-2-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-35-7P, 2-[[4'-[5-Methyl-1H-indol-1-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-36-8P, 2-[[4'-[3-(Butylamino)imidazo[1,2-a]pyridin-2-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-37-9P, Methyl 2-[[4'-[(2-benzoylphenoxy)methyl]biphenyl-4-yl]oxy]-2-phenylacetate 796033-38-0P, Methyl 2-[[4'-[(2-benzylphenyl)oxy]methyl]biphenyl-4-yl]oxy]-2-phenylacetate 796033-39-1P, Methyl 2-[[4'-[(9H-fluoren-2-yloxy)methyl]biphenyl-4-yl]oxy]-2-phenylacetate 796033-40-4P, Methyl 2-[[4'-[(3-benzoylphenyl)oxy]methyl]biphenyl-4-yl]oxy]-2-phenylacetate 796033-41-5P, 2-[[4'-[(3-Benzoylphenoxy)methyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-42-6P, 2-[[4'-[(2-Benzoylphenoxy)methyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-43-7P, 2-[[4'-[(1-Butylindolizin-2-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-44-8P, 2-[4-(1-Benzyl-1H-indol-6-yl)phenoxy]-2-(phenyl)acetic acid 796033-45-9P, 2-[[4'-[10-(Ethoxycarbonyl)pyrido[1,2-a]indol-3-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-46-0P, 2-[[4'-[Benzo[b]furan-2-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-47-1P, 2-[[4'-[1H-Indol-1-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-48-2P, Methyl 2-[[4'-[1-benzyl-1H-indol-6-yl]biphenyl-4-yl]oxy]-2-phenylacetate 796033-49-3P, 2-[[4'-[1-Benzyl-1H-indol-6-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-50-6P, 2-[[4'-[1-Benzyl-1H-indol-5-yl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-58-4P, 2-[[4'-[(2-Butylbenzo[b]furan-3-yl)methyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-63-1P, 2-[[2'-(1,3-Benzoxazol-2-yl)-1,1':4',1''-terphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-64-2P, 2-[[4'-[(2-Butylbenzo[b]furan-3-yl)carbonyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-78-8P, 2-[[4'-[Benzo[b]thien-2-yl]biphenyl-4-yl]oxy]-2-

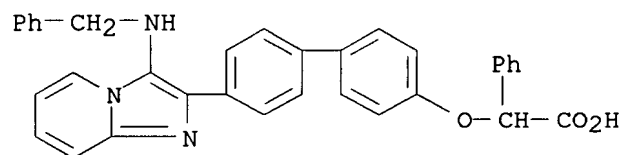
(phenyl)acetic acid 796033-80-2P, 2-[[4'-(Dibenzo[b,d]furan-4-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-81-3P, 2-[[4'-(n-Butyl)-1,1':4',1''-terphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-83-5P, 2-[[4'-[(2-Benzyl-7-fluorobenzo[b]furan-3-yl)carbonyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-94-8P, 2-[[4'-[(9-Oxo-9H-fluoren-1-yl)oxy]methyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-95-9P, Methyl 2-[[4'-(benzo[b]furan-2-yl)biphenyl-4-yl]oxy]-2-phenylacetate 796033-97-1P, 2-[[4'-(Benzo[b]thien-3-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796033-98-2P, Methyl 2-[[4'-(1-benzyl-1H-indol-5-yl)biphenyl-4-yl]oxy]-2-phenylacetate 796034-05-4P, 2-[[4'-(Dibenzothiophen-4-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-10-1P, 2-[[4'-(5-Chloroindol-1-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-11-2P, 2-[[3-Chloro-4'-(dibenzofuran-4-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-12-3P, 2-[[4'-(Dibenzofuran-4-yl)-2-methylbiphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-13-4P, 2-[[4'-(Dibenzofuran-4-yl)-3-fluorobiphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-14-5P, 2-[[2-Chloro-4'-(dibenzofuran-4-yl)biphenyl-4-yl]oxy]-2-(phenyl)acetic acid 796034-15-6P, 2-[[4'-(Dibenzofuran-4-yl)-2-trifluoromethylbiphenyl-4-yl]oxy]-2-(phenyl)acetic acid

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PTP-1B inhibitor; preparation of substituted carboxylic acids as PTP-1B inhibitors for treatment of diabetes, cancer, and related conditions)

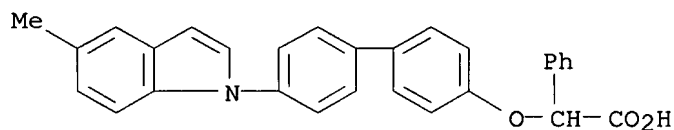
RN 796033-34-6 CAPLUS

CN Benzeneacetic acid, α -[[4'-[3-[(phenylmethyl)amino]imidazo[1,2-a]pyridin-2-yl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



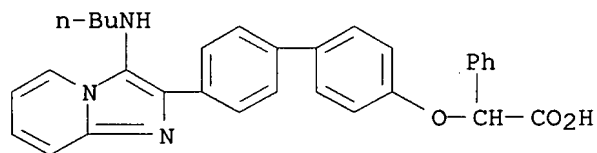
RN 796033-35-7 CAPLUS

CN Benzeneacetic acid, α -[[4'-(5-methyl-1H-indol-1-yl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



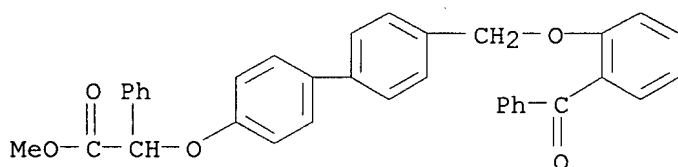
RN 796033-36-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-[3-(butylamino)imidazo[1,2-a]pyridin-2-yl][1,1'-biphenyl]-4-yl]oxy]- (9CI) (CA INDEX NAME)



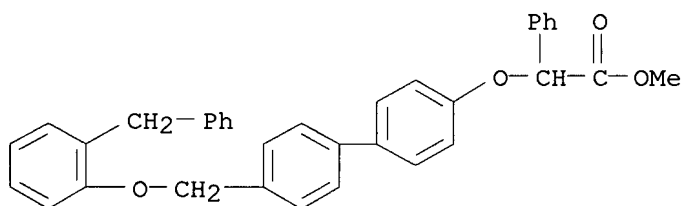
RN 796033-37-9 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(2-benzoylphenoxy)methyl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



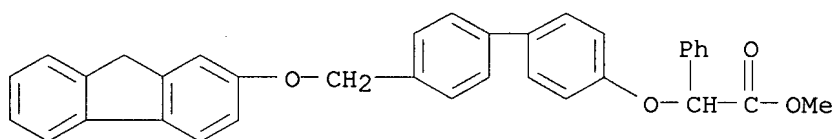
RN 796033-38-0 CAPLUS

CN Benzeneacetic acid, α -[[4'-[[2-(phenylmethyl)phenoxy]methyl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



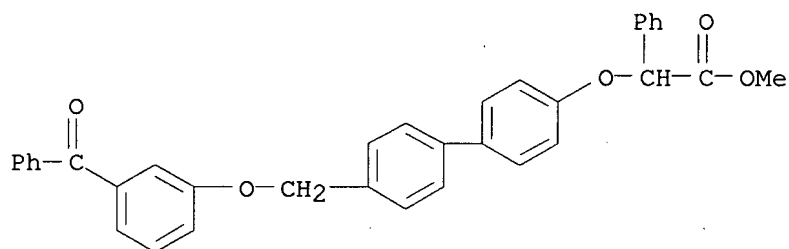
RN 796033-39-1 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(9H-fluoren-2-yloxy)methyl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



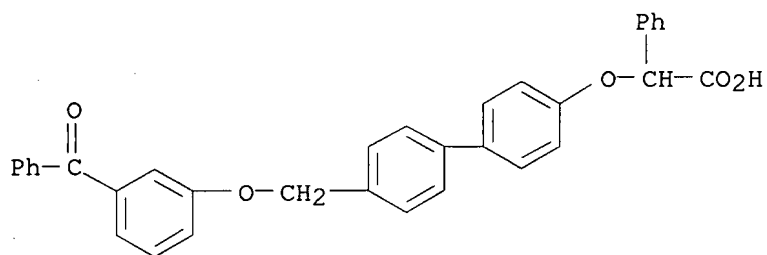
RN 796033-40-4 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(3-benzoylphenoxy)methyl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



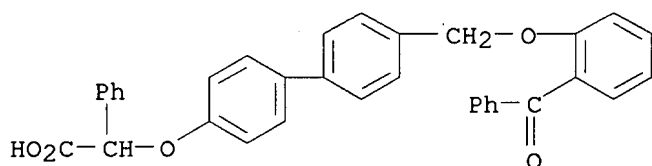
RN 796033-41-5 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(3-benzoylphenoxy)methyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



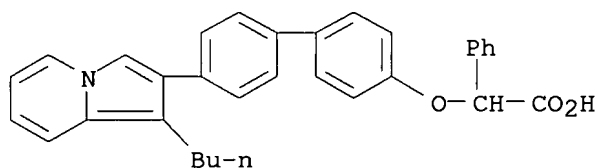
RN 796033-42-6 CAPLUS

CN Benzeneacetic acid, α-[[4'-[(2-benzoylphenoxy)methyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



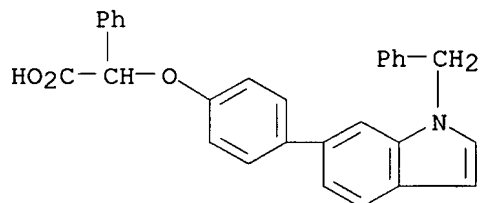
RN 796033-43-7 CAPLUS

CN Benzeneacetic acid, α-[[4'-(1-butyl-2-indoliziny)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



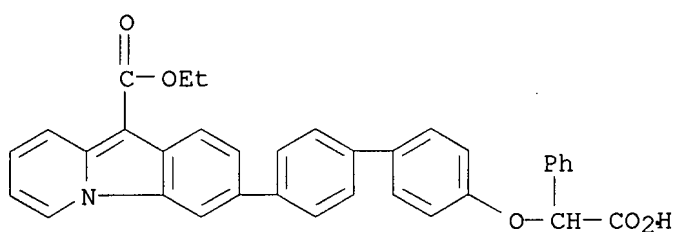
RN 796033-44-8 CAPLUS

CN Benzeneacetic acid, α-[4-[1-(phenylmethyl)-1H-indol-6-yl]phenoxy]- (CA INDEX NAME)



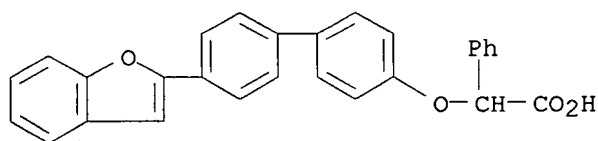
RN 796033-45-9 CAPLUS

CN Pyrido[1,2-a]indole-10-carboxylic acid, 3-[4'-(carboxyphenylmethoxy)[1,1'-biphenyl]-4-yl]-, 10-ethyl ester (CA INDEX NAME)



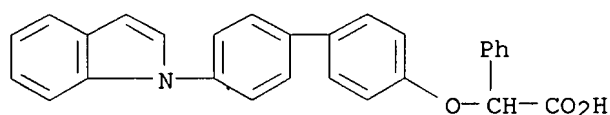
RN 796033-46-0 CAPLUS

CN Benzeneacetic acid, α-[[4'-(2-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]-
(CA INDEX NAME)



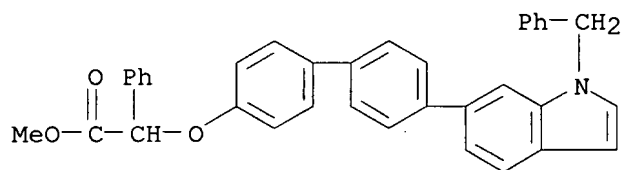
RN 796033-47-1 CAPLUS

CN Benzeneacetic acid, α-[[4'-(1H-indol-1-yl)[1,1'-biphenyl]-4-yl]oxy]-
(CA INDEX NAME)



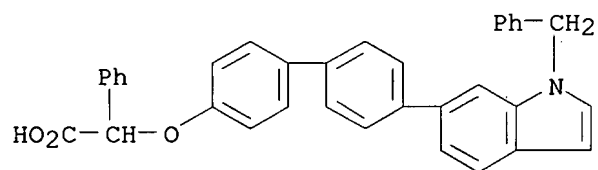
RN 796033-48-2 CAPLUS

CN Benzeneacetic acid, α-[[4'-[1-(phenylmethyl)-1H-indol-6-yl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



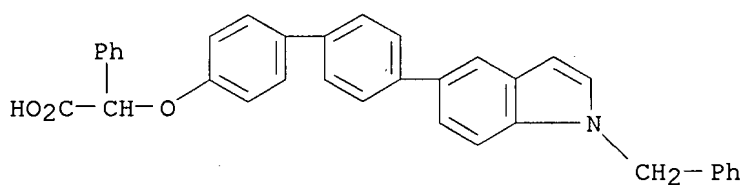
RN 796033-49-3 CAPLUS

CN Benzeneacetic acid, α-[[4'-[1-(phenylmethyl)-1H-indol-6-yl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



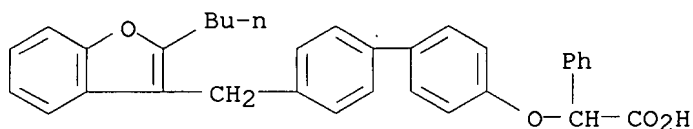
RN 796033-50-6 CAPLUS

CN Benzeneacetic acid, α-[[4'-[1-(phenylmethyl)-1H-indol-5-yl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



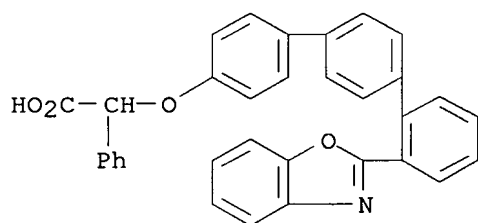
RN 796033-58-4 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(2-butyl-3-benzofuranyl)methyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



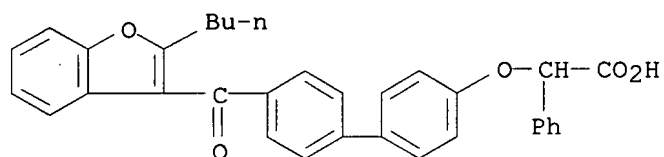
RN 796033-63-1 CAPLUS

CN Benzeneacetic acid, α -[[2'-(2-benzoxazolyl)[1,1':4',1''-terphenyl]-4-yl]oxy]- (9CI) (CA INDEX NAME)



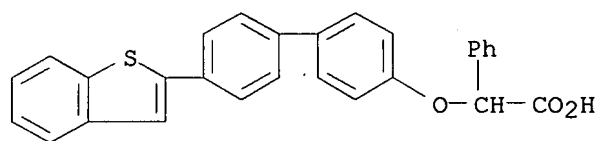
RN 796033-64-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(2-butyl-3-benzofuranyl)carbonyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



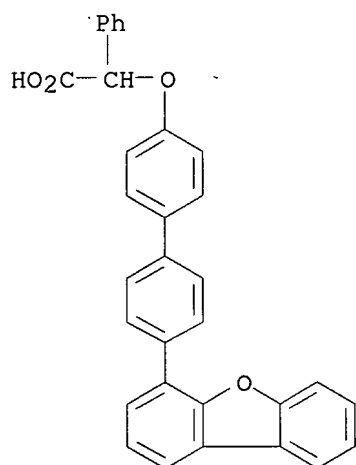
RN 796033-78-8 CAPLUS

CN Benzeneacetic acid, α -[(4'-benzo[b]thien-2-yl[1,1'-biphenyl]-4-yl)oxy]- (CA INDEX NAME)



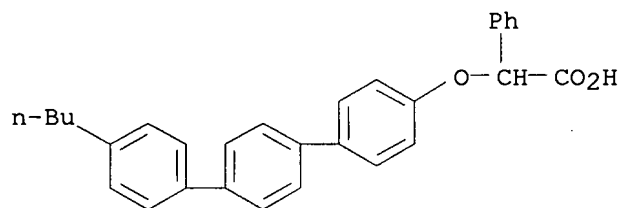
RN 796033-80-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-(4-dibenzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



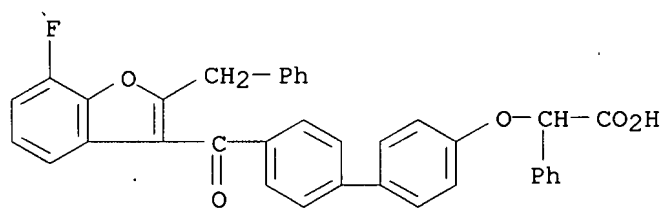
RN 796033-81-3 CAPLUS

CN Benzeneacetic acid, α -[(4''-butyl[1,1':4',1''-terphenyl]-4-yl)oxy]- (9CI) (CA INDEX NAME)



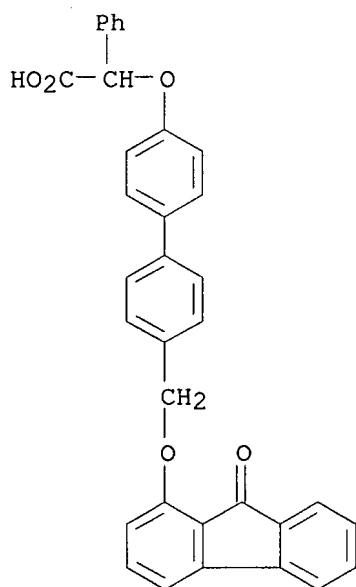
RN 796033-83-5 CAPLUS

CN Benzeneacetic acid, α -[[4'-[[7-fluoro-2-(phenylmethyl)-3-benzofuranyl]carbonyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



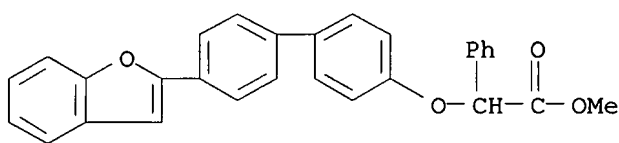
RN 796033-94-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-[[[9-oxo-9H-fluoren-1-yl]oxy]methyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



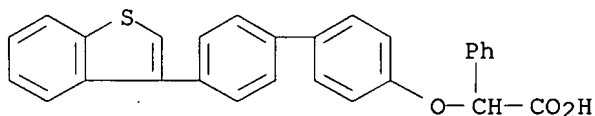
RN 796033-95-9 CAPLUS

CN Benzeneacetic acid, α -[4'-(2-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



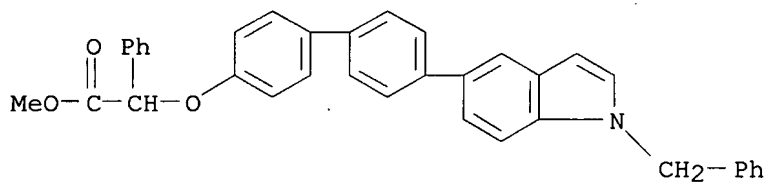
RN 796033-97-1 CAPLUS

CN Benzeneacetic acid, α -[4'-benzo[b]thien-3-yl[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



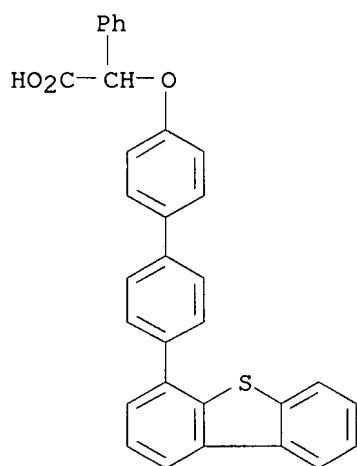
RN 796033-98-2 CAPLUS

CN Benzeneacetic acid, α -[4'-[1-(phenylmethyl)-1H-indol-5-yl][1,1'-biphenyl]-4-yl]oxy]-, methyl ester (CA INDEX NAME)



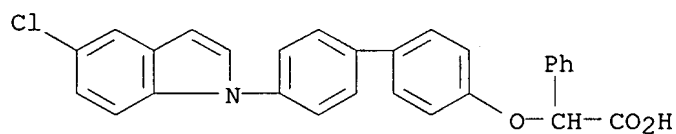
RN 796034-05-4 CAPLUS

CN Benzeneacetic acid, α -[4'-(4-dibenzothienyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



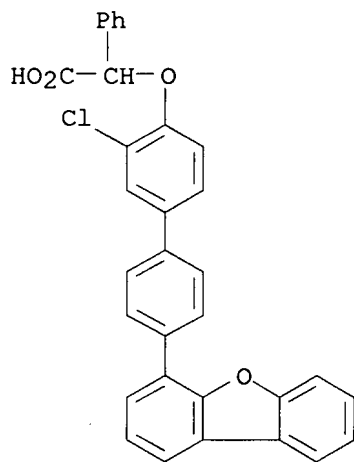
RN 796034-10-1 CAPLUS

CN Benzeneacetic acid, α -[4'-(5-chloro-1H-indol-1-yl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



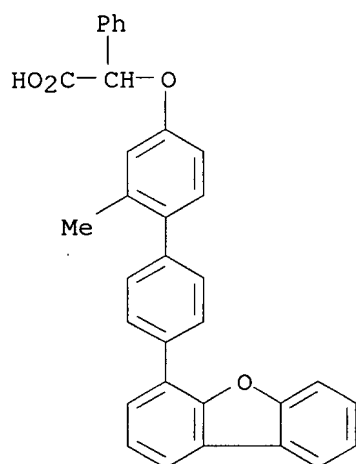
RN 796034-11-2 CAPLUS

CN Benzeneacetic acid, α -[3-chloro-4'-(4-dibenzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



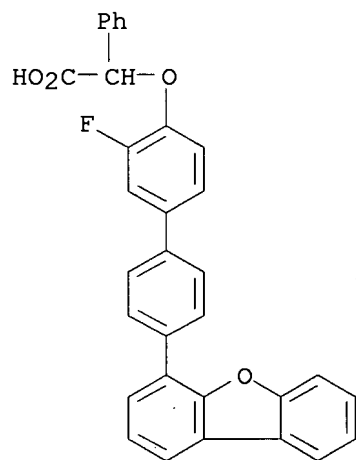
RN 796034-12-3 CAPLUS

CN Benzeneacetic acid, α -[4'-(4-dibenzofuranyl)-2-methyl[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



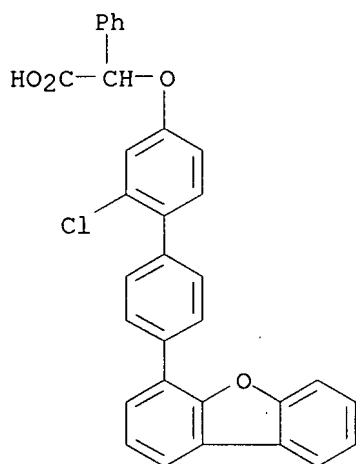
RN 796034-13-4 CAPLUS

CN Benzeneacetic acid, α -[[4'-(4-dibenzofuranyl)-3-fluoro[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)

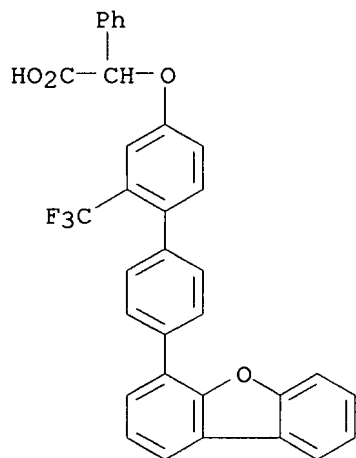


RN 796034-14-5 CAPLUS

CN Benzeneacetic acid, α -[[2-chloro-4'-(4-dibenzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



RN 796034-15-6 CAPLUS
 CN Benzeneacetic acid, α -[[4'-(4-dibenzofuranyl)-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



L4 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:961757 CAPLUS
 DOCUMENT NUMBER: 142:348095
 TITLE: 3D-QSAR of protein tyrosine phosphatase 1B inhibitors by genetic function approximation
 AUTHOR(S): Vadlamudi, Sree M.; Kularni, Vithal M.
 CORPORATE SOURCE: Inst. Chem. Technol., Dep. Pharmaceutical Sci. Technol., Univ. Mumbai, Mumbai, 400019, India
 SOURCE: Internet Electronic Journal of Molecular Design (2004), 3(9), 586-609
 CODEN: IEJMAT; ISSN: 1538-6414
 URL: ftp://biochempress.com/iejmd_2004_3_0586.pdf
 PUBLISHER: BioChem Press
 DOCUMENT TYPE: Journal; (online computer file)
 LANGUAGE: English
 AB Protein tyrosine phosphatase 1B (PTP 1B) has been implicated as neg. regulator of insulin receptor signaling system. Design of small mol. PTP 1B inhibitors has received considerable attention as inhibition of PTP 1B enzyme is expected to improve insulin action, to treat non-insulin dependent diabetes mellitus (NIDDM). In this work, we report three

dimensional quant. structure activity relationship (3D-QSAR) study performed by genetic function approximation (GFA) technique on a series of benzofuran/benzothiophene biphenyls as PTP 1B inhibitors. The QSAR models were generated using 92 compds., and the predictive ability of the resulting each model was evaluated against a test set of 26 compds. The internal (correlation coefficient r2) and external consistency (predictive r2) of the final QSAR model was 0.694 and 0.672 resp. Analyses of results from the present QSAR study indicate that electronic, structural, and shape descriptors govern the PTP 1B inhibitory activity.

IT 263759-84-8

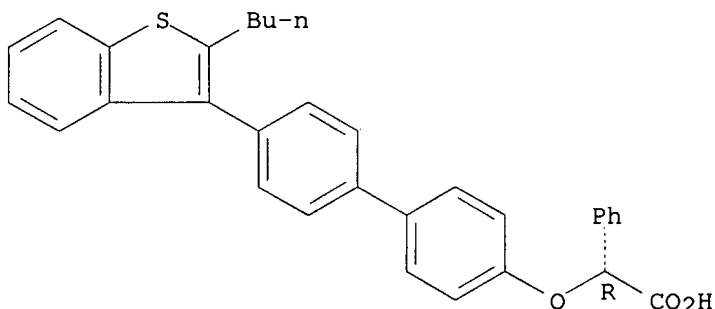
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(3D-QSAR anal. by genetic function approximation on protein tyrosine phosphatase 1B inhibitors targeting diabetes in human revealed electronic, structural and shape descriptors accounts for this effect)

RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:701969 CAPLUS

DOCUMENT NUMBER: 141:207209

TITLE: Preparation of substituted imidazoles as protein tyrosine phosphatase inhibitors for treatment of diabetes and other PTPase mediated conditions

INVENTOR(S): Mjalli, Adnan M. M.; Andrews, Robert C.; Yarragunta, Ravindra R.; Xie, Rongyuan; Subramanian, Govindan; Quada, James C., Jr.; Arimilli, Murty N.; Polisetti, Dharma R.

PATENT ASSIGNEE(S): Transtech Pharma Inc., USA

SOURCE: PCT Int. Appl., 281 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

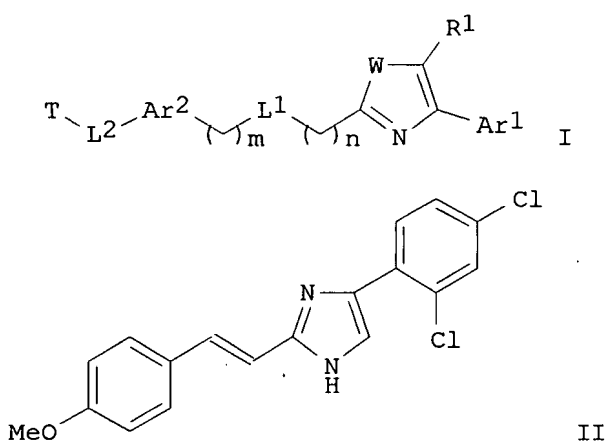
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071447	A2	20040826	WO 2004-US4074	20040212
WO 2004071447	A3	20041223		
WO 2004071447	B1	20050310		
WO 2004071447	A9	20051013		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
 BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
 MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2004210711 A1 20040826 AU 2004-210711 20040212
 CA 2514363 A1 20040826 CA 2004-2514363 20040212
 US 2004192743 A1 20040930 US 2004-777488 20040212
 EP 1594847 A2 20051116 EP 2004-710607 20040212
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1747936 A 20060315 CN 2004-80004085 20040212
 JP 2006518738 T 20060817 JP 2006-503512 20040212
 PRIORITY APPLN. INFO.: US 2003-446977P P 20030212
 WO 2004-US4074 W 20040212
 OTHER SOURCE(S): MARPAT 141:207209
 GI



AB Title imidazoles and analogs I [wherein m, n = independently 0-2; W = O, S, NR2; R1 = H, halo, CN, alkyl, (hetero)aryl, heterocyclyl, etc.; R2 = H, alkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), etc.; Ar1 = (un)substituted optionally fused (hetero)aryl; Ar2 = (un)substituted optionally fused (hetero)arylene; L1 = a bond, (un)substituted ethylene, NHCO, NH, NHSO2, etc.; L2 = CH2, O, alkylene, (hetero)arylene, etc.; T = H, (un)substituted (cyclo)alkyl, heterocyclyl, (hetero)aryl, etc.; and pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as inhibitors of protein tyrosine phosphatases (PTPases). For example, reaction of trans-4-methoxycinnamic acid with 2,4-dichlorophenacyl bromide in the presence of DIEA in DMF gave the keto-ester (no data), which was treated with ammonium acetate in glacial AcOH to afford (E)-II (56%). Compds. of the invention inhibited PTP 1B activity with IC50 values ranging from about 0.01 μ M to about 20 μ M. Thus, I and pharmaceutical compns. comprising them may be useful for the management, treatment, control, and adjunct treatment of diseases mediated by PTPase activity, such as Type I diabetes, Type II diabetes, immune dysfunction, AIDS, autoimmune diseases, glucose intolerance, obesity, cancer, psoriasis, allergic diseases, infectious diseases, inflammatory diseases, diseases involving the modulated synthesis and/or production of growth hormone or cytokines, of Alzheimer's disease (no data).
 IT 744237-61-4P, 2-[[4'-[2-[4-(2,4-Dichlorophenyl)-1-ethyl-1H-imidazol-2-yl]-(E)-ethenyl]biphenyl-4-yl]oxy]-2-(phenyl)acetic acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

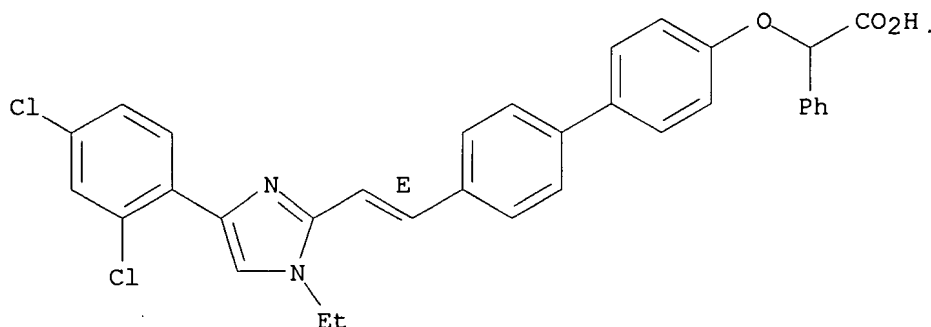
(Uses)

(PTPase inhibitor; preparation of substituted imidazoles as PTPase inhibitors for treatment of diabetes and other PTPase mediated conditions)

RN 744237-61-4 CAPLUS

CN Benzeneacetic acid, α -[[4'-[(1E)-2-[4-(2,4-dichlorophenyl)-1-ethyl-1H-imidazol-2-yl]ethenyl][1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)

Double bond geometry as shown.



L4 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:777734 CAPLUS

DOCUMENT NUMBER: 139:292242

TITLE: Preparation of heteroarylphenoxyphenylacetates for treating diseases associated with glucose metabolism, lipid metabolism and insulin secretion.

INVENTOR(S): Zhao, Zuchun; Chen, Xin; Wang, Jianchao; Sun, Hongbin; Liang, Jack Shih-Chieh

PATENT ASSIGNEE(S): Metabolex, Inc., USA

SOURCE: PCT Int. Appl., 330 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080545	A2	20031002	WO 2003-US8899	20030319
WO 2003080545	A3	20040122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2004DN03020	A	20070105	IN 2004-DN3020	20011004
CA 2479338	A1	20031002	CA 2003-2479338	20030319
AU 2003237787	A1	20031008	AU 2003-237787	20030319
US 2004029933	A1	20040212	US 2003-394487	20030319
US 7078421	B2	20060718		
EP 1487843	A2	20041222	EP 2003-736445	20030319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008537	A	20050209	BR 2003-8537	20030319

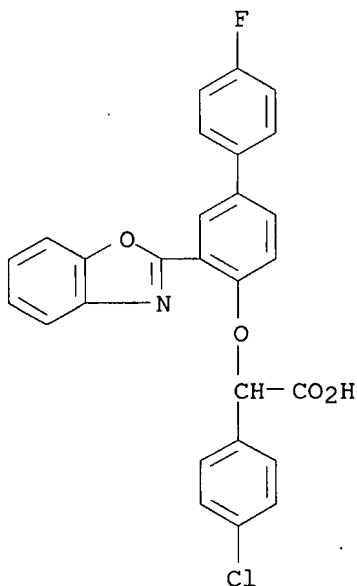
IT 609350-47-2P 609350-48-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heteroarylphenoxyphenylacetates for treating diseases associated with glucose metabolism, lipid metabolism and insulin secretion)

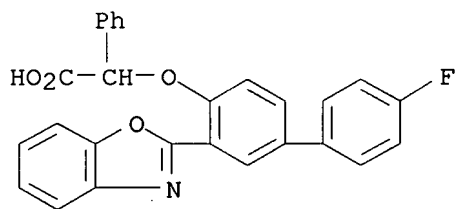
RN 609350-47-2 CAPLUS

CN Benzeneacetic acid, α -[[3-(2-benzoxazolyl)-4'-fluoro[1,1'-biphenyl]-4-yl]oxy]-4-chloro- (CA INDEX NAME)



RN 609350-48-3 CAPLUS

CN Benzeneacetic acid, α -[[3-(2-benzoxazolyl)-4'-fluoro[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



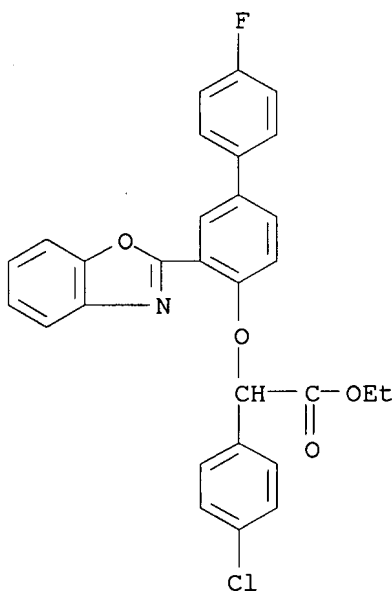
IT 609352-36-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of heteroarylphenoxyphenylacetates for treating diseases associated with glucose metabolism, lipid metabolism and insulin secretion)

RN 609352-36-5 CAPLUS

CN Benzeneacetic acid, α -[[3-(2-benzoxazolyl)-4'-fluoro[1,1'-biphenyl]-4-yl]oxy]-4-chloro-, ethyl ester (CA INDEX NAME)



L4 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:702655 CAPLUS

DOCUMENT NUMBER: 140:53160

TITLE: Applications of genetic algorithms on 2D-QSAR analysis of benzofuran and benzothiophene biphenyls as PTP1B inhibitors

AUTHOR(S): Pan, Yong-Mei; Ji, Ming-Juan

CORPORATE SOURCE: Graduate School, Chinese Academy of Sciences, Beijing, 100039, Peop. Rep. China

SOURCE: Wuli Huaxue Xuebao (2003), 19(8), 695-700

CODEN: WHXUEU; ISSN: 1000-6818

PUBLISHER: Beijing Daxue Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Quant. structure-activity relationships (QSARs) for 43 benzofuran and benzothiophene biphenyls were studied. By using a genetic algorithm (GA), a group of multiple regression models with high fitness scores (r^2 was up to 0.70) were generated. From the statistical analyses of the descriptors used in the evolution procedure, four of them, including the partition coefficient (1 gP), the mol. surface area (Area), the mol. weight (MW), and the dipole vector (Dip) were found to be the principal features affecting the biol. activity. For example, the mol. surface area appeared in 94% of the models in the elite populations. That is to say, the hydrophobic interactions between the inhibitors and the receptors are very important to the biol. activity, which supplies a guide for the design and reconstruction of new PTP1B inhibitors.

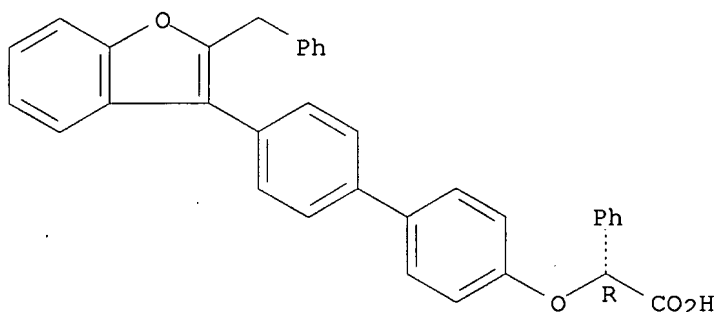
IT 250341-99-2 263759-84-8

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(applications of genetic algorithms on 2D-QSAR anal. of benzofuran and benzothiophene biphenyls types of PTP1B inhibitors as antidiabetic agents for Diabetes mellitus treatment)

RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

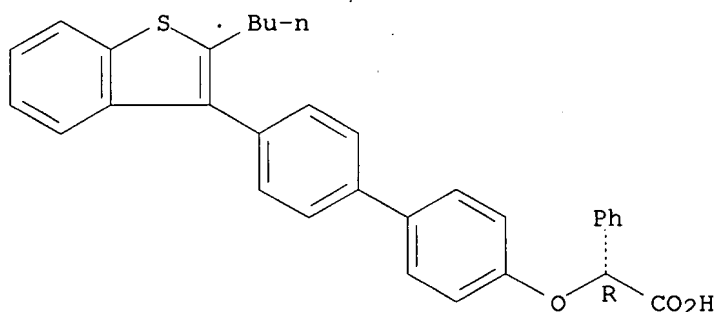
Absolute stereochemistry.



RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:101319 CAPLUS

DOCUMENT NUMBER: 139:159427

TITLE: 3D-QSAR analyses of novel benzofuranyl and benzothiophenyl biphenyls as PTP1B inhibitors

AUTHOR(S): Pan, Yong-Mei; Ji, Ming-Juan; Ye, Xue-Qi; Kuang, Ping-Xian

CORPORATE SOURCE: Graduate School of Chinese Academy of Science, Beijing, 100039, Peop. Rep. China

SOURCE: Youji Huaxue (2003), 23(2), 167-172

CODEN: YCHHDX; ISSN: 0253-2786

PUBLISHER: Kexue Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Comparative mol. field anal. (CoMFA) was performed to study the structure-activity relationship of novel benzofuranyl and benzothiophenyl biphenyls as protein tyrosine phosphatase 1B (PTP1B) inhibitors. In this anal., three mol. fields were considered: electrostatic field, steric field and H-bond field. The value of cross-validated coefficient q^2 was found to be 0.58, showing that the model from CoMFA was good and the predictive biol. activity of mols. in the test set indicated the predictive potential of the model for the untested compds. It also indicated that the addition of H-bond field did improve the quality of the QSAR model. From anal. of the CoMFA coefficient contour plots, steric and electrostatic properties were identified, which were very helpful for designing new compds. In addition, a newly developed approach, comparative mol. similarity indexes anal. (CoMSIA), was tried. However, the results show that CoMSIA does not lead to any improvement compared with CoMFA for the system examined in this work.

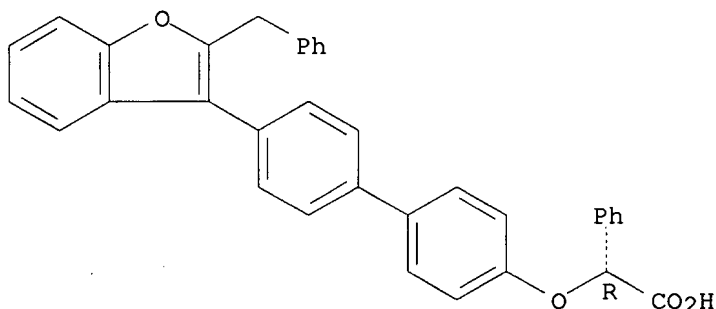
IT 250341-99-2 263759-84-8

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3D-QSAR analyses of novel benzofuranyl and benzothiophenyl biphenyls as PTP1B inhibitors)

RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

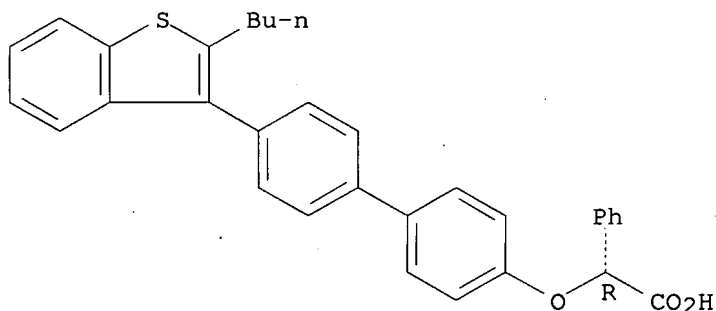
Absolute stereochemistry.



RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:671733 CAPLUS

DOCUMENT NUMBER: 137:201154

TITLE: Preparation of phenyl derivatives as inhibitors of factor Xa and factor VIIa

INVENTOR(S): Cezanne, Bertram; Juraszyk, Horst; Dorsch, Dieter; Tsaklakidis, Chistos; Gleitz, Johannes; Barnes, Christopher

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: Ger. Offen., 20 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

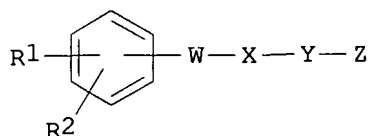
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10110325	A1	20020905	DE 2001-10110325	20010303
CA 2439644	A1	20020912	CA 2002-2439644	20020204

WO 2002070471	A1	20020912	WO 2002-EP1114	20020204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002250878	A1	20020919	AU 2002-250878	20020204
EP 1370522	A1	20031217	EP 2002-719754	20020204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003003437	A2	20040128	HU 2003-3437	20020204
JP 2004525119	T	20040819	JP 2002-569792	20020204
CN 1524072	A	20040825	CN 2002-805731	20020204
MX 2003PA07866	A	20031204	MX 2003-PA7866	20030901
US 2004092517	A1	20040513	US 2003-469687	20030903
ZA 2003007715	A	20050103	ZA 2003-7715	20031002
PRIORITY APPLN. INFO.:			DE 2001-10110325	A 20010303
			WO 2002-EP1114	W 20020204
OTHER SOURCE(S):		MARPAT 137:201154		
GI				

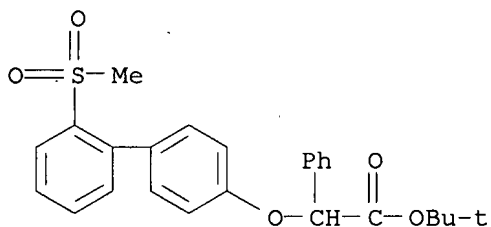


AB Title compds. [I; R1 = cyano, COR3, CO2R3, OR3, (amino protecting group-substituted) C(:NH)NH2, CON(R3)2, etc.; R2 = H, halo, A, OR3, N(R3)2, NO2, cyano, CO2R3, CON(R3)2, etc.; R3 = H, A, etc.; A = (branched) (O-, S-interrupted) (fluorinated) alkyl, alkenyl; W = NR3CO, NR3COC(R4)2, NR3C(R4)2, C(R4)2NR3C(R4)2; R4 = H, A; X = C(R3)2, [C(R3)2]2, C(R3)2O, C(R3)2NR3; Y = alkylene, cycloalkylene, (substituted) heterocycldiyl, etc; Z = OR3, N(R3)2, N(R3)2CON(R3)2, etc.], were prepared Thus, a mixture of (rac)-2-(2'-methanesulfonylbiphenyl-4-oxy)-2-phenylacetic acid (preparation given), 3-(methyl-1,2,4-oxadiazol-3-yl)aniline, and TBTU in DMF was stirred with 4-methylmorpholine for 20 h at room temperature to give (rac)-N-[3-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-2-(2'-methanesulfonylbiphenyl-4-oxy)-2-phenylacetamide which was hydrogenated in the presence of Raney Ni for 18 h at room temperature to give (rac)-N-(3-amidinophenyl)-2-(2'-methanesulfonylbiphenyl-4-oxy)-2-phenylacetamide. The latter inhibited factor Xa with IC50 = 1.1·10⁻⁷ M and factor VIIa with IC50 = 4.6·10⁻⁸ M.

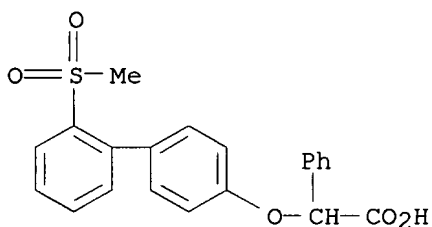
IT 452314-25-9P 452314-28-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of amidinophenyls as inhibitors of factor Xa and factor VIIa)

RN 452314-25-9 CAPLUS

CN Benzeneacetic acid, α-[[2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]oxy]-, 1,1-dimethylethyl ester (CA INDEX NAME)

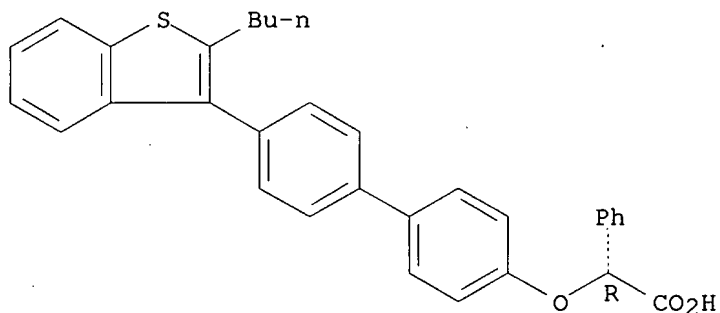


RN 452314-28-2 CAPLUS
 CN Benzeneacetic acid, α -[[2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]oxy]-
 (CA INDEX NAME)



L4 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:324943 CAPLUS
 DOCUMENT NUMBER: 137:319942
 TITLE: 3D-QSAR CoMFA and CoMSIA on protein tyrosine phosphatase 1B inhibitors
 AUTHOR(S): Murthy, V. Sreenivasa; Kulkarni, Vithal M.
 CORPORATE SOURCE: Pharmaceutical Technology and Pharmacy Division, Institute of Chemical Technology, University of Mumbai, Matunga, Mumbai, 400 019, India
 SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(7), 2267-2282
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB 3D-QSAR and mol. modeling was performed on a series of benzofuran/benzothiophene biphenyls as protein tyrosine phosphatase 1B (PTP 1B) inhibitors with anti-hyperglycemic activity. Evaluation of 92 compds. served to establish the model, which was validated by evaluation of an external set of 26 compds. The lowest energy conformer of most active compound obtained from simulated annealing was used as a template structure for the alignment. The best predictions were obtained with the CoMFA model from RMS fit and A log P as addnl. descriptor ($r^2_{cv}=0.615$, $r^2=0.842$), and with the CoMSIA combined steric, electrostatic, and lipophilic fields ($r^2_{cv}=0.597$, $r^2=0.910$). The 3D-QSAR model was then superimposed to the PTP 1B active site, giving direct contour maps of the different fields. Further comparison of the contour maps from the 3D-QSAR showed high level of compatibility with the active site of PTP 1B enzyme.
 IT 263759-84-8
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (3D-QSAR CoMFA and CoMSIA on protein tyrosine phosphatase 1B inhibitors)
 RN 263759-84-8 CAPLUS
 CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

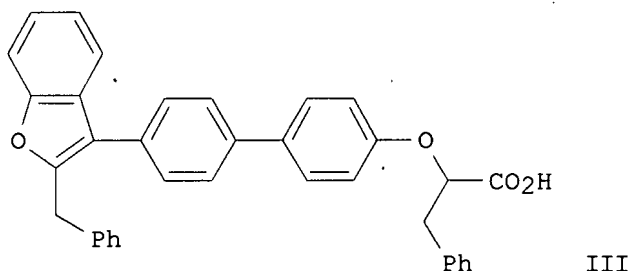
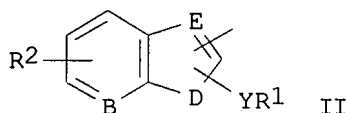
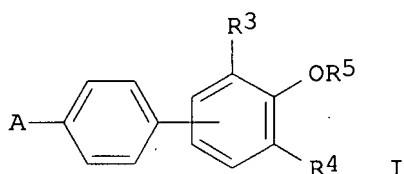
Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:355085 CAPLUS
DOCUMENT NUMBER: 134:353250
TITLE: Preparation of α -(biphenylyloxo)alkanoic acids
for treatment of insulin resistance and hyperglycemia
INVENTOR(S): Malamas, Michael S.; Mcdevitt, Robert E.; Adebayo,
Folake O.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 30 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6232322	B1	20010515	US 1999-307972	19990510
US 2001041715	A1	20011115	US 2001-798109	20010302
US 6391897	B2	20020521		
US 2001053785	A1	20011220	US 2001-798088	20010302
US 6369072	B2	20020409		
PRIORITY APPLN. INFO.:			US 1998-113654P	P 19980512
			US 1998-76205	A 19980512
			US 1999-307972	A3 19990510
OTHER SOURCE(S):	MARPAT 134:353250			
GI				



AB The title compds. [I; A = II (wherein B = C; D = O, S, N; E = C; Y = a bond, CH₂; CO, CHO; R₁ = alkyl, aryl, arylakyl, etc.; R₂ = H, alkyl, alkoxy, etc.); R₃, R₄ = H, halo, alkyl, etc.; R₅ = H, alkyl, etc.] were prepared as protein-tyrosine phosphatase inhibitors. Thus, 4-BrC₆H₄COCH₂Br was etherified by PhOH and the cyclized product condensed with 4-(MeO)C₆H₄B(OH)₂ to give, after O-demethylation, 3-(4'-hydroxybiphenyl)benzofuran which was acylated by BzNMeOMe and the reduced product etherified by (R)-PhCH₂CH(OH)CO₂Me to give, after saponification,

title compd (S)-III. Data for biol. activity of I were given.

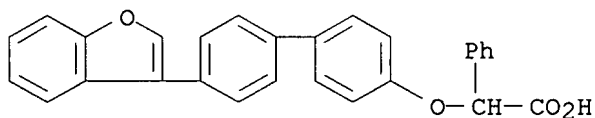
IT 250341-86-7P 250341-99-2P 250342-02-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of α-(biphenyloxy)alkanoic acids for treatment of insulin resistance and hyperglycemia)

RN 250341-86-7 CAPLUS

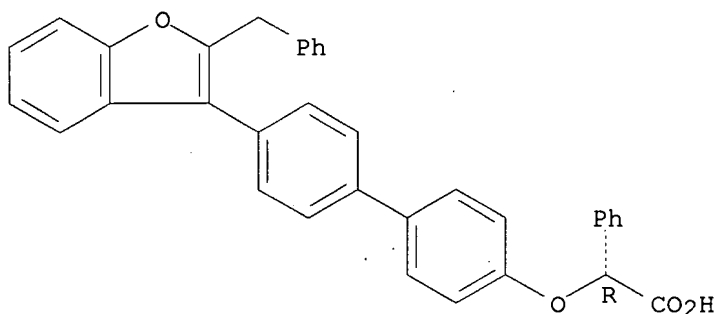
CN Benzeneacetic acid, α-[[4'-(3-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



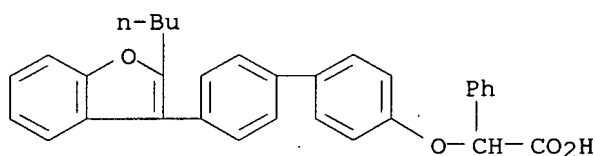
RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α-[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-biphenyl]-4-yl]oxy]-, (αR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 250342-02-0 CAPLUS
 CN Benzeneacetic acid, α-[[4'-(2-butyl-3-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)

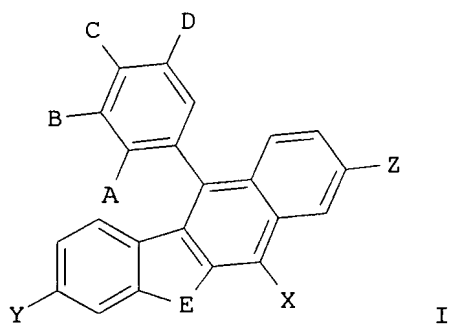


REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:607330 CAPLUS
 DOCUMENT NUMBER: 133:193067
 TITLE: Preparation of 11-aryl-benzo[b]naphtho[2,3-d]furans and 11-aryl-benzo[b]naphtho[2,3-d]thiophenes for treating insulin resistance and hyperglycemia
 INVENTOR(S): Wrobel, Jay E.; Dietrich, Arlene J.; Li, Zenan
 PATENT ASSIGNEE(S): American Home Products Corporation, USA
 SOURCE: U.S., 67 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

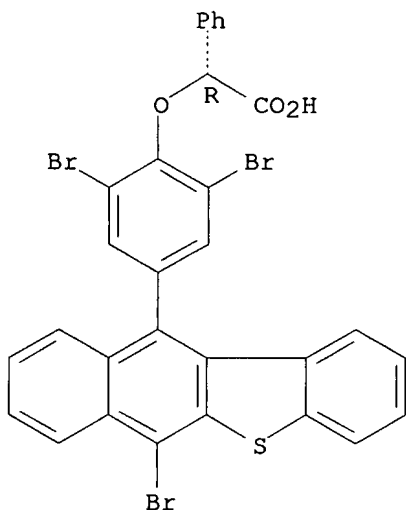
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6110962	A	20000829	US 1999-307840	19990510
PRIORITY APPLN. INFO.:			US 1998-98554P	P 19980512
OTHER SOURCE(S):		MARPAT 133:193067		

GI



- AB The title compds. [I; A = H, halo, OH; B, D = H, halo, CN, etc.; E = S, SO, SO₂, O; X = H, halo, alkyl, etc.; Y, Z = H, OR₂; R₂ = H, alkyl, aralkyl, CH₂CO₂R₃; R₃ = H, alkyl; C = H, halo, OR₄; R₄ = H, alkyl, CH(R₅)W, etc.; R₅ = H, alkyl, aralkyl, etc.; W = CONH₂, CONHOH, CN, etc.; with the proviso that at least one of A-D is not H atom] and their pharmaceutically acceptable salts, which are useful in treating insulin resistance and hyperglycemia, were prepared E.g., a multi-step synthesis of I [A, B, D = H; C = OH; E = S; X, Y, Z = H] which showed -34.19% change from control in test for PTPase inhibition at 50 μ M, was given.
- IT 250350-80-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of 11-aryl-benzo[b]naphtho[2,3-d]furans and 11-aryl-benzo[b]naphtho[2,3-d]thiophenes for treating insulin resistance and hyperglycemia)
- RN 250350-80-2 CAPLUS
- CN Benzeneacetic acid, α -[2,6-dibromo-4-(6-bromobenzo[b]naphtho[2,3-d]thien-11-yl)phenoxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:128048 CAPLUS
 DOCUMENT NUMBER: 132:273845

TITLE: Novel Benzofuran and Benzothiophene Biphenyls as Inhibitors of Protein Tyrosine Phosphatase 1B with Antihyperglycemic Properties

AUTHOR(S): Malamas, Michael S.; Sredy, Janet; Moxham, Christopher; Katz, Alan; Xu, Weixin; McDevitt, Robert; Adebayo, Folake O.; Sawicki, Diane R.; Seestaller, Laura; Sullivan, Donald; Taylor, Joseph R.

CORPORATE SOURCE: Wyeth-Ayerst Research Inc., Princeton, NJ, 08543-8000, USA

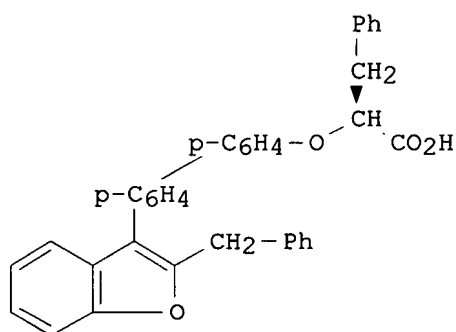
SOURCE: Journal of Medicinal Chemistry (2000), 43(7), 1293-1310
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Insulin resistance in the liver and peripheral tissues, together with a pancreatic cell defect, are the common causes of Type 2 diabetes. It is now appreciated that insulin resistance can result from a defect in the insulin receptor signaling system, at a site post binding of insulin to its receptor. Protein tyrosine phosphatases (PTPases) have been shown to be neg. regulators of the insulin receptor. Inhibition of PTPases may be an effective method in the treatment of Type 2 diabetes. We have identified two novel series of benzofuran/benzothiophene biphenyl oxo-acetic acids and sulfonyl-salicylic acids as potent inhibitors of PTP1B with good oral antihyperglycemic activity. To assist in the design of these inhibitors, crystallog. studies have attempted to identify enzyme inhibitor interactions. Resolution of crystal complexes has suggested that the inhibitors bind to the enzyme active site and are held in place through hydrogen bonding and van der Waals interactions formed within two hydrophobic pockets. In the oxo-acetic acid series, hydrophobic substituents at position-2 of the benzofuran/benzothiophene biphenyl framework interacted with Phe182 of the catalytic site and were very critical to the intrinsic activity of the mol. The hydrophobic region of the catalytic-site pocket was exploited and taken advantage by hydrophobic substituents at either the α -carbon or the ortho aromatic positions of the oxo-acetic acid moiety. Similar ortho aromatic substitutions on the salicylic acid-type inhibitors had no effect, primarily due to the different orientation of these inhibitors in the catalytic site. The most active inhibitors of both series inhibited recombinant human PTP1B with phosphotyrosyl dodecapeptide TRDI(P)YETD(P)Y(P)YRK as the source of the substrate with IC₅₀ values in the range of 20-50 nM. Compound I was one of the most active compds. in vivo, normalizing plasma glucose levels at the

25 mg/kg dose (po) and the 1 mg/kg dose (i.p.). Compound I was also selective against several other PTPases.

IT 250341-99-2P

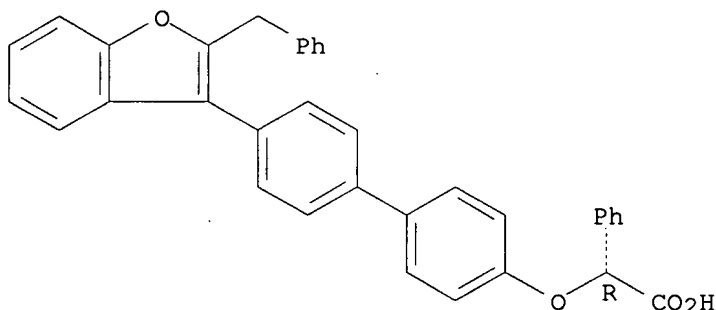
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis of benzofuran and benzothiophene biphenyls as inhibitors of protein tyrosine phosphatase 1B with antihyperglycemic properties)

RN 250341-99-2 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-(phenylmethyl)-3-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 263759-84-8P

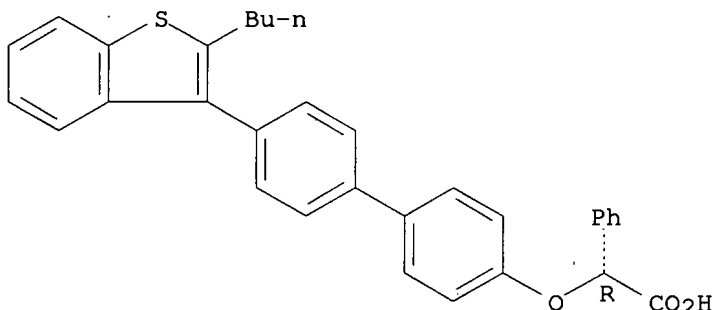
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of benzofuran and benzothiophene biphenyls as inhibitors of protein tyrosine phosphatase 1B with antihyperglycemic properties)

RN 263759-84-8 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butylbenzo[b]thien-3-yl)[1,1'-biphenyl]-4-yl]oxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

43

THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:736689 CAPLUS

DOCUMENT NUMBER: 131:351227

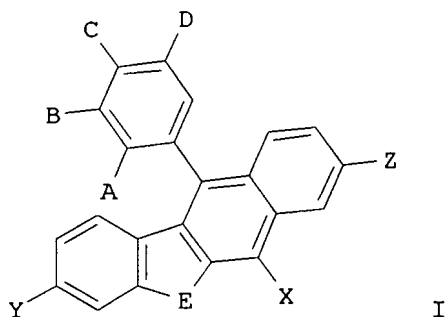
TITLE: Preparation of 11-aryl-benzo[b]naphtho[2,3-d]furans and 11-aryl-benzo[b]naphtho[2,3-d]thiophenes useful in the treatment of insulin resistance and hyperglycemia

INVENTOR(S): Wrobel, Jay Edward; Dietrich, Arlene Joan; Li, Zenan

PATENT ASSIGNEE(S): American Home Products Corp., USA

SOURCE: PCT Int. Appl., 209 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958521	A1	19991118	WO 1999-US10185	19990510
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330623	A1	19991118	CA 1999-2330623	19990510
AU 9939791	A	19991129	AU 1999-39791	19990510
EP 1077970	A1	20010228	EP 1999-922897	19990510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002514638	T	20020521	JP 2000-548325	19990510
MX 2000PA11089	A	20010405	MX 2000-PA11089	20001110
PRIORITY APPLN. INFO.:			US 1998-76592	A 19980512
			WO 1999-US10185	W 19990510
OTHER SOURCE(S):		MARPAT 131:351227		
GI				



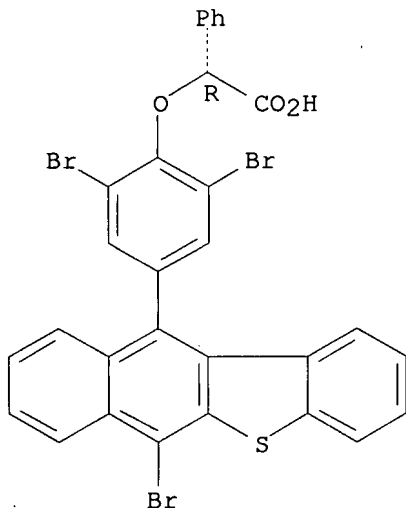
AB The title compds. [I; A = H, halo, OH; B, D = H, halo, CN, etc.; E = S, SO, SO₂, O; X = H, halo, alkyl, etc.; Y, Z = H, OR₂; R₂ = H, alkyl, aralkyl, etc.; C = H, halo, OR₄; R₄ = H, alkyl, 5-thiazolidine-2,4-dione, etc.] and their pharmaceutically acceptable salts, which are useful in treating metabolic disorders related to insulin resistance or hyperglycemia, were prepared. Thus, treatment of 4-benzo[b]naphtho[2,3-d]thiophen-11-ylphenol and KOAc in AcOH with a solution of Br₂ in glacial AcOH afforded I [E = S; Y = Z = H; X = Br; A = H; B = D = Br; C = OH] which showed IC₅₀ of 0.384 μ M against human recombinant PTP1B.

IT 250350-80-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of 11-aryl-benzo[b]naphtho[2,3-d]furans and 11-aryl-benzo[b]naphtho[2,3-d]thiophenes useful in the treatment of insulin resistance and hyperglycemia)

RN 250350-80-2 CAPLUS
CN Benzeneacetic acid, α -[2,6-dibromo-4-(6-bromobenzo[b]naphtho[2,3-d]thien-11-yl)phenoxy]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

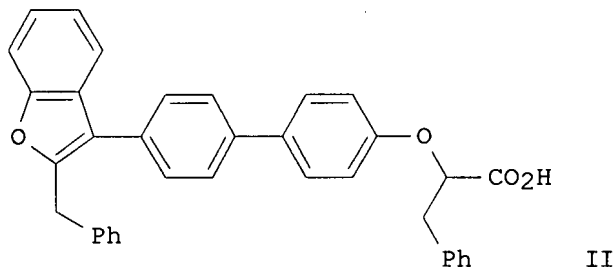
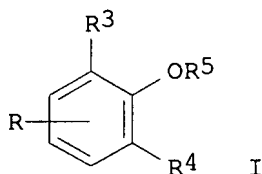
L4 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:736685 CAPLUS
DOCUMENT NUMBER: 131:351222
TITLE: Preparation of α -(biphenylyloxo)alkanoic acids for treatment of insulin resistance and hyperglycemia
INVENTOR(S): Malamas, Michael Sotirios; McDevitt, Robert Emmett; Adebayo, Folake Oluwemimo
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958518	A2	19991118	WO 1999-US10201	19990510
WO 9958518	A3	20000120		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2330557	A1	19991118	CA 1999-2330557	19990510
AU 9941836	A	19991129	AU 1999-41836	19990510
EP 1077967	A2	20010228	EP 1999-925583	19990510
EP 1077967	B1	20021204		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
JP 2002514635	T	20020521	JP 2000-548322	19990510

AT 229015
MX 2000PA11086
PRIORITY APPLN. INFO.:

T 20021215
A 20010405
OTHER SOURCE(S):
GI
MARPAT 131:351222

AT 1999-925583 19990510
MX 2000-PA11086 20001110
US 1998-76205 A 19980512
WO 1999-US10201 W 19990510



AB Title compds. [I; R = 4-(R¹Z¹Z²)C₆H₄; R¹ = (ar)alkyl, alkoxy, (hetero)aryl, etc.; Z¹ = bond, CH₂, CO, CH(OH); Z² = (benz)imidazolylene, (benzo)furylene, thienylene, etc.; R³, R⁴ = H, halo, alkyl, alkoxy, etc.; R⁵ = H, alkyl, CH₂CO₂H, CHR₈CH₂CO₂H, etc.; R₈ = H, (ar)alkyl, aryl, etc.] were prepared as protein-tyrosine phosphatase inhibitors. Thus, 4-BrC₆H₄COCH₂Br was etherified by PhOH and the cyclized product condensed with 4-(MeO)C₆H₄B(OH)₂ to give, after O-demethylation, 3-(4'-hydroxybiphenyl)benzofuran which was acylated by BzNMeOMe and the reduced product etherified by (R)-PhCH₂CH(OH)CO₂Me to give, after saponification,

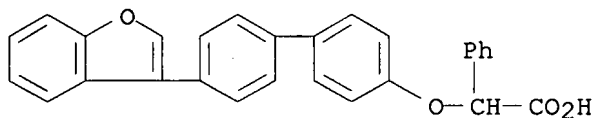
title compd (S)-II. Data for biol. activity of I were given.

IT 250341-86-7P 250341-99-2P 250342-02-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-(biphenyloxy)alkanoic acids for treatment of insulin resistance and hyperglycemia)

RN 250341-86-7 CAPLUS

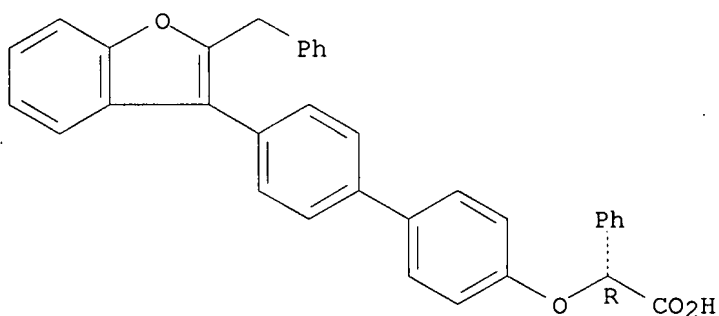
CN Benzeneacetic acid, α-[[4'-(3-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]-
(CA INDEX NAME)



RN 250341-99-2 CAPLUS

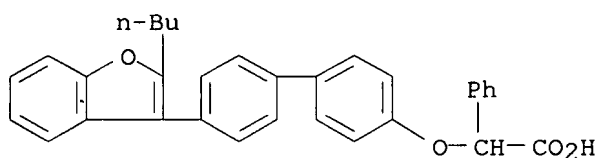
CN Benzeneacetic acid, α-[[4'-[2-(phenylmethyl)-3-benzofuranyl][1,1'-biphenyl]-4-yl]oxy]-, (αR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 250342-02-0 CAPLUS

CN Benzeneacetic acid, α -[[4'-(2-butyl-3-benzofuranyl)[1,1'-biphenyl]-4-yl]oxy]- (CA INDEX NAME)



L4 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:87469 CAPLUS

DOCUMENT NUMBER: 90:87469

ORIGINAL REFERENCE NO.: 90:13872h,13873a

TITLE: Azolylalkanecarboxylic acid derivatives

INVENTOR(S): Thomas, Rudolf; Kraemer, Wolfgang; Buechel, Karl Heinz; Paul, Volker; Frohberger, Paul Ernst

PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 48 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

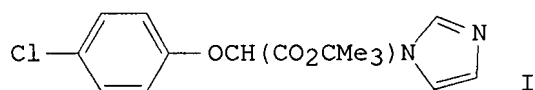
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2720654	A1	19781116	DE 1977-2720654	19770507
GB 1568350	A	19800529	GB 1978-17482	19780503
IL 54637	A	19821231	IL 1978-54637	19780504
BE 866718	A1	19781106	BE 1978-187402	19780505
DK 7801979	A	19781108	DK 1978-1979	19780505
NL 7804859	A	19781109	NL 1978-4859	19780505
FR 2389617	A1	19781201	FR 1978-13361	19780505
FR 2389617	B1	19830114		
BR 7802840	A	19790123	BR 1978-2840	19780505
CH 638793	A5	19831014	CH 1978-4926	19780505
JP 53137959	A	19781201	JP 1978-53310	19780506
PRIORITY APPLN. INFO.:			DE 1977-2720654	A 19770507

GI



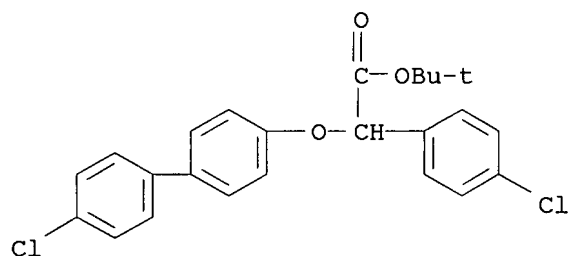
AB ROCR1R2COR3 (R = optionally substituted Ph, alkyl; R1 = optionally substituted azolyl; R2 = H, optionally substituted Ph, alkyl; R3 = alkoxy, cycloalkoxy, optionally substituted phenoxy, amino) were prepared Thus, 4-ClC6H4OH was treated with ClCH2CO2CMe3 and the resulting 4-ClC6H4OCH2CO2CMe3 brominated to give 4-ClC6H4OCHBrCO2CMe3, which was treated with imidazole to give I. At 0.025% I protected rice against *Pyricularia oryzae*.

IT 69335-80-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and bromination of)

RN 69335-80-4 CAPLUS

CN Benzeneacetic acid, 4-chloro- α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

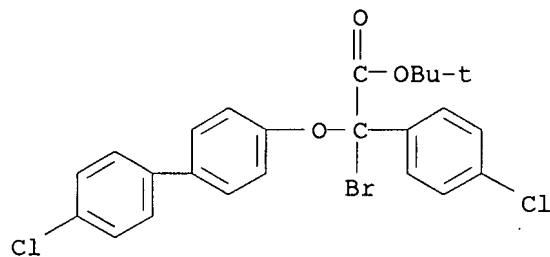


IT 69335-66-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with azoles)

RN 69335-66-6 CAPLUS

CN Benzeneacetic acid, α -bromo-4-chloro- α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

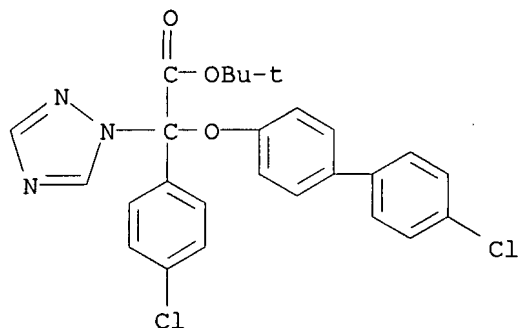


IT 69335-25-7P 69335-47-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

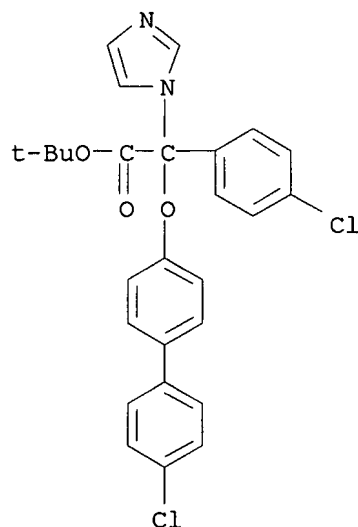
RN 69335-25-7 CAPLUS

CN 1H-1,2,4-Triazole-1-acetic acid, α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]- α -(4-chlorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 69335-47-3 CAPLUS

CN 1H-Imidazole-1-acetic acid, α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]- α -(4-chlorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1975:496755 CAPLUS

DOCUMENT NUMBER: 83:96755

ORIGINAL REFERENCE NO.: 83:15181a,15184a

TITLE: Hydratropic acid derivatives

INVENTOR(S): Schacht, Erich; Mehrhof, Werner; Simane, Zdenek;
Nowak, Herbert; Kayser, Detlev

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Fed. Rep. Ger.

SOURCE: Ger. Offen., 29 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2358789	A1	19750605	DE 1973-2358789	19731126
ZA 7405890	A	19750924	ZA 1974-5890	19740917
CA 1059516	A1	19790731	CA 1974-213692	19741114
AU 7475405	A	19760520	AU 1974-75405	19741115
CS 176295	B2	19770630	CS 1974-8625	19741120
BE 822496	A1	19750522	BE 1974-150763	19741122
SE 7414704	A	19750527	SE 1974-14704	19741122

FR 2252093	A1	19750620	FR 1974-38453	19741122
FR 2252093	B1	19780908		
JP 50083345	A	19750705	JP 1974-136099	19741125
DK 7406131	A	19750728	DK 1974-6131	19741125
GB 1435050	A	19760512	GB 1974-50946	19741125
US 4072754	A	19780207	US 1974-527089	19741125
CH 605589	A5	19780929	CH 1974-15633	19741125
CH 605590	A5	19780929	CH 1977-14185	19741125
AT 351538	B	19790725	AT 1974-9432	19741125
AT 7409432	A	19790115		
NL 7415414	A	19750528	NL 1974-15414	19741126
HU 168666	B	19760628	HU 1974-ME1801	19741126
DD 114399	A5	19750812	DD 1975-182563	19751125
CS 176290	B2	19770630	CS 1976-7936	19761120
CS 176294	B2	19770630	CS 1976-8624	19761120
AT 7705438	A	19790615	AT 1977-5438	19770726
AT 354449	B	19790110		
AT 7705439	A	19790615	AT 1977-5439	19770726
AT 354450	B	19790110		
CH 617172	A5	19800514	CH 1977-14186	19771121
PRIORITY APPLN. INFO.:			DE 1973-2358789	A 19731126
			AT 1974-9432	A 19741125
			CH 1974-15633	19741125

OTHER SOURCE(S): MARPAT 83:96755

AB 4-RC6H4OCMePhCO2H (I; R = e.g., H, Cl, Ph, 4-ClC6H4O, 1-pyrrolyl, 1,2,3,4-tetrahydro-4-quinolyl) were prepared by the reaction of 4-RC6H4OH with PhCMeBrCO2Et and Na in MeOH, followed by saponification Salts and esters of

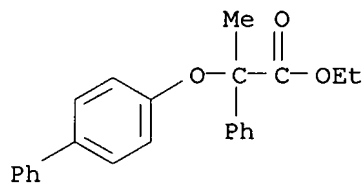
I were also prepared I were useful as cholesterol- and triglyceride-lowering agents; ED data were given.

IT 56855-26-6P 56855-27-7P 56855-38-0P
56855-39-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

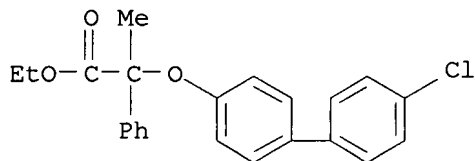
RN 56855-26-6 CAPLUS

CN Benzeneacetic acid, α -([1,1'-biphenyl]-4-yloxy)- α -methyl-, ethyl ester (9CI) (CA INDEX NAME)



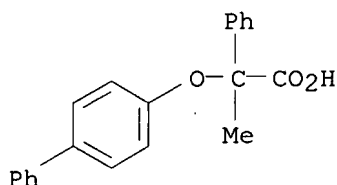
RN 56855-27-7 CAPLUS

CN Benzeneacetic acid, α -(4'-chloro[1,1'-biphenyl]-4-yloxy)- α -methyl-, ethyl ester (9CI) (CA INDEX NAME)

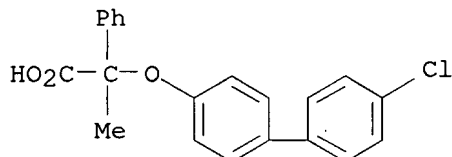


RN 56855-38-0 CAPLUS

CN Benzeneacetic acid, α -([1,1'-biphenyl]-4-yloxy)- α -methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 56855-39-1 CAPLUS
 CN Benzeneacetic acid, α -(4'-chloro[1,1'-biphenyl]-4-yloxy)- α -methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1975:31275 CAPLUS
 DOCUMENT NUMBER: 82:31275
 ORIGINAL REFERENCE NO.: 82:4969a, 4972a
 TITLE: Phenoxyacetic acid derivatives
 INVENTOR(S): Schacht, Erich; Mehrhof, Werner; Nowak, Herbert;
 Simane, Zdenek; Kayser, Detlev
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H.
 SOURCE: Ger. Offen., 32 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2312344	A1	19740919	DE 1973-2312344	19730313
ZA 7401400	A	19750226	ZA 1974-1400	19740304
HU 168080	B	19760228	HU 1974-ME1715	19740307
US 3992386	A	19761116	US 1974-449332	19740308
BE 812121	A1	19740911	BE 1974-141858	19740311
FR 2221135	A1	19741011	FR 1974-8184	19740311
DD 110494	A5	19741220	DD 1974-177100	19740311
GB 1422926	A	19760128	GB 1974-10723	19740311
NL 7403309	A	19740917	NL 1974-3309	19740312
JP 49125358	A	19741130	JP 1974-28996	19740312
AU 7466547	A	19750918	AU 1974-66547	19740312
ES 424179	A1	19770116	ES 1974-424179	19740312
AT 7402044	A	19770415	AT 1974-2044	19740312
AT 340420	B	19771212		
ES 446532	A1	19771016	ES 1976-446532	19760331
SE 7605082	A	19760504	SE 1976-5082	19760504
US 4053626	A	19771011	US 1976-724232	19760917
PRIORITY APPLN. INFO.:			DE 1973-2312344	A 19730313
			DE 1973-2319642	A 19730418
			DE 1973-2325184	A 19730518
			US 1974-449332	A3 19740308

GI For diagram(s), see printed CA Issue.

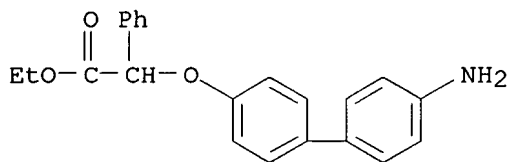
AB Twenty-six (cyclic amino)phenoxyacetic acids and their esters I (R = H, Me, Et, Pr, CH₂CHMe₂, CMe₃; R₁ = Me, Ph, ClC₆H₄; R₂ = 1-pyrrolyl, piperidino, isoindolyl, 1,2,3,4-tetrahydro-1-quinolyl, its 4-quinolyl isomer and 4-quinolyl isomer 1-Me derivative, 4-piperidinophenyl and -phenoxy), with blood cholesterol-, glyceride, and -uric acid-lowering properties, were prepared from (cyclic amino)phenols and R₃CHR₁CO₂R (R₃ = Br, Cl), or from III (Z = direct bond, p-C₆H₄O, or p-C₆H₄) and Br(CH₂)₅Br, or by the hydrolysis or esterification of IV (R₅ = CN, CONH₂, COCl). Thus, 4-piperidinophenol was added to Na in EtOH and the mixture treated with Et 2-bromo-2-phenylacetate and refluxed 10 hr to give I (R = Et, R₁ = Ph, R₂ = piperidino) HCl salt. Saponification of the free base gave the acid

(I, R = H). Reaction of III (R = Et, R₁ = Me, Z = p-C₆H₄O) with Br(CH₂)₅Br in BuOH-K₂CO₃ gave Et 2-[4-(4-piperidinophenoxy)-phenoxy]propionate. Hydrolysis of IV (R₁ = p-ClC₆H₄, R₂ = 1,2,3,4-tetrahydro-1-quinolyl, R₅ = CN) 2 hr in AcOH-concentrated HCl under N gave the acetic acid derivative

IT 54395-31-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cyclization with dibromopentane)

RN 54395-31-2 CAPLUS

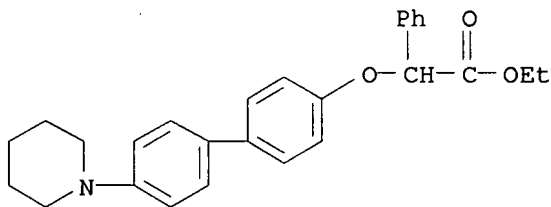
CN Benzeneacetic acid, α-[(4'-amino[1,1'-biphenyl]-4-yl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



IT 54394-98-8P 54394-99-9P 54395-00-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

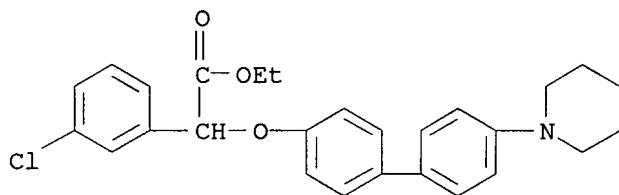
RN 54394-98-8 CAPLUS

CN Benzeneacetic acid, α-[[4'-(1-piperidinyl)[1,1'-biphenyl]-4-yl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)

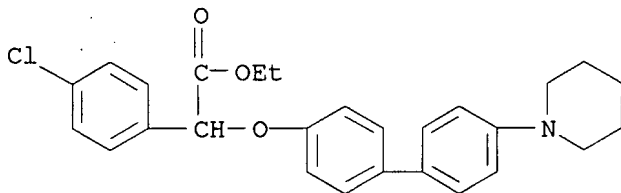


RN 54394-99-9 CAPLUS

CN Benzeneacetic acid, 3-chloro-α-[[4'-(1-piperidinyl)[1,1'-biphenyl]-4-yl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



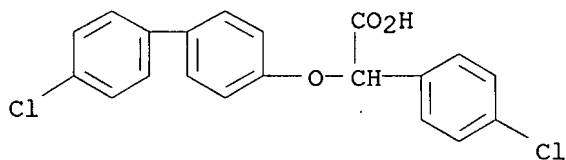
RN 54395-00-5 CAPLUS
 CN Benzeneacetic acid, 4-chloro- α -[[4'-(1-piperidiny)[1,1'-biphenyl]-4-yl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



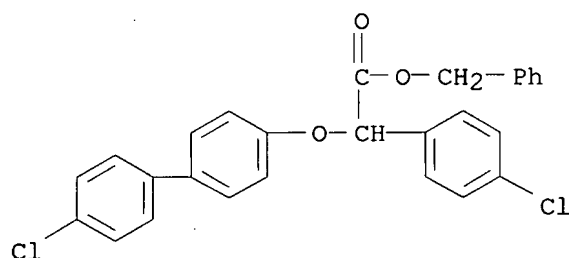
L4 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:536854 CAPLUS
 DOCUMENT NUMBER: 79:136854
 ORIGINAL REFERENCE NO.: 79:22173a,22176a
 TITLE: Amides and esters of phenoxyphenylacetic acids
 INVENTOR(S): Bolhofer, William A.
 PATENT ASSIGNEE(S): Merck and Co., Inc.
 SOURCE: Ger. Offen., 33 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2307038	A1	19730906	DE 1973-2307038	19730213
NL 7301246	A	19730816	NL 1973-1246	19730129
CH 587794	A5	19770513	CH 1973-1901	19730209
JP 48086842	A	19731115	JP 1973-16667	19730212
GB 1388776	A	19750326	GB 1973-6789	19730212
FR 2181725	A1	19731207	FR 1973-4988	19730213
			US 1972-226293	A 19720214

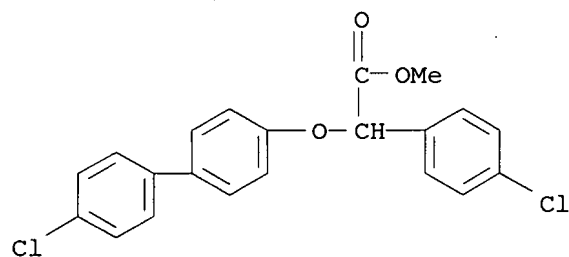
PRIORITY APPLN. INFO.:
 AB Seven RC6H4OCH(COR1)C6H4R2-4 [I; R = 3-allyl, 3-CF3, 4-PrCO, 4-PhNH, 4-ClC6H4, 4-(1,2,3,4-tetrahydro-1-naphthyl); R1 = OCH2CH2NHAc, OCH2CH2NHBr, NHCH2CO2H, NHCH2CH2Cl, OCH2Ph; R2 = Cl, OMe] and salts with cyclohexylamine or citric acid, useful as anticholesteremics, blood fat lowering drugs, and in the treatment of atherosclerosis, were prepared mainly by treatment of I (R1 = OH) with SOCl2 to give I (R1 = Cl) and reaction with alcs. and amines. Thus, I (R = 4-PrCO, R1 = OH, R2 = Cl) and SOCl2 were refluxed in CHCl3 to give the chloride, which reacted with HOCH2CH2NHAc in DMF and Et2O in the presence of pyridine at from 5° to room temperature to give I (R = 4-PrCO, R1 = OCH2CH2NHAc, R2 = Cl).
 IT 50819-85-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (amidation and esterification of)
 RN 50819-85-7 CAPLUS
 CN Benzeneacetic acid, 4-chloro- α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]- (9CI) (CA INDEX NAME)



IT 50819-87-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and pharmacol. activity of)
 RN 50819-87-9 CAPLUS
 CN Benzeneacetic acid, 4-chloro- α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT 50819-84-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 50819-84-6 CAPLUS
 CN Benzeneacetic acid, 4-chloro- α -[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:93101 CAPLUS

DOCUMENT NUMBER: 64:93101

ORIGINAL REFERENCE NO.: 64:17471e-f

TITLE: Influence of molecular structure on optical properties of systems with carbon asymmetry centers. V. On synthesis of optically active α -(4-biphenyloxy)phenylacetic acids

AUTHOR(S): Janczewski, Marian; Bilczuk, Luba

CORPORATE SOURCE: Skłodowska Curie Univ., Lublin, Pol.

SOURCE: Roczniki Chemii (1965), 39(12), 1927-9

CODEN: ROCHAC; ISSN: 0035-7677

DOCUMENT TYPE: Journal

LANGUAGE: French

AB cf. CA 60, 14416c. 4-Hydroxybiphenyl heated with the Me ether of α -bromophenylacetic acid (I) and MeONa in anhydrous MeOH medium gave Me α -(4-diphenyloxy)phenylacetate, m. 119-20° (MeOH). I treated with MeOH + H₂O solution of KOH gave racemic α -(4-diphenyloxy)phenylacetic acid (II), m. 181-2° amide m. 208-9°; p-nitrobenzyl ether m. 145-6°, p-bromo-phenacyl ether m. 121-2°. II was separated by fractional crystallization of neutral

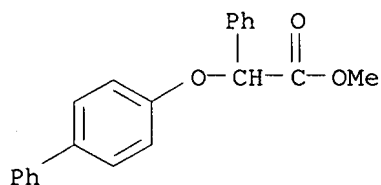
salts of cinchonidine into optical antipodes, m. 195-6° with $[\alpha]_{20D} -106.06$, and m. 194-5° with $[\alpha]_{20D} 106.06$. Similarly, racemic α -(4-diphenyloxy)propionic acid was obtained, m. 165-6°. cf. CA 62, 16159g.

IT 5555-10-2 5555-18-0 5555-19-1
7522-98-7

(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 5555-10-2 CAPLUS

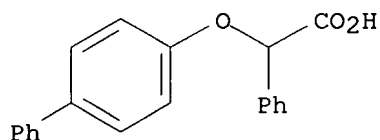
CN Benzeneacetic acid, α -([1,1'-biphenyl]-4-yloxy)-, methyl ester (9CI)
(CA INDEX NAME)



RN 5555-18-0 CAPLUS

CN Benzeneacetic acid, α -([1,1'-biphenyl]-4-yloxy)-, (-)- (9CI) (CA INDEX NAME)

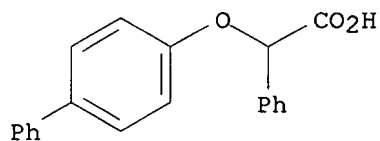
Rotation (-).



RN 5555-19-1 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl-, (\pm)- (8CI) (CA INDEX NAME)

Rotation (+).



RN 7522-98-7 CAPLUS

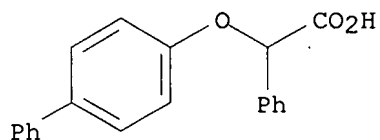
CN Cinchonan-9-ol, (8 α ,9R)-, mono[(-)- α -([1,1'-biphenyl]-4-yloxy)benzeneacetate] (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 5555-18-0

CMF C20 H16 O3

Rotation (-).

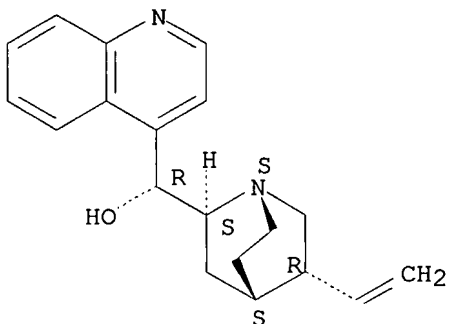


CM 2

CRN 485-71-2

CMF C19 H22 N2 O

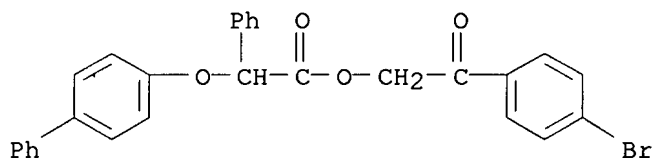
Absolute stereochemistry. Rotation (-).



IT 5555-12-4P, Acetic acid, (4-biphenyloxy)phenyl-, ester with 4'-bromo-2-hydroxyacetophenone 5999-18-8P, Acetic acid, (4-biphenyloxy)phenyl-, p-nitrobenzyl ester 94465-08-4P, Acetic acid, (4-biphenyloxy)phenyl-, (-), (+)- 106336-82-7P, Acetic acid, (4-biphenyloxy)phenyl-, compound with cinchonidine (1:1) 881738-34-7P, Cinchonidine, (4-biphenyloxy)phenylacetate
RL: PREP (Preparation)
(preparation of)

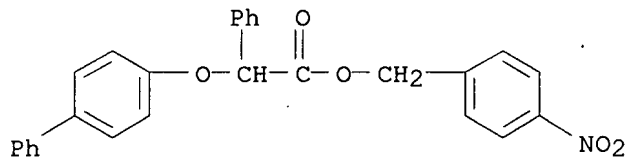
RN 5555-12-4 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl-, ester with 4'-bromo-2-hydroxyacetophenone (7CI, 8CI) (CA INDEX NAME)



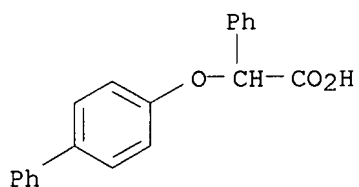
RN 5999-18-8 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl-, p-nitrobenzyl ester (7CI, 8CI) (CA INDEX NAME)



RN 94465-08-4 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl- (7CI) (CA INDEX NAME)



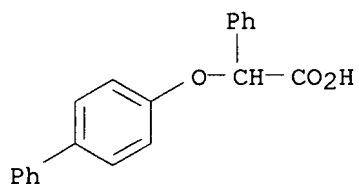
RN 106336-82-7 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl-, compd. with cinchonidine (7CI) (CA INDEX NAME)

CM 1

CRN 94465-08-4

CMF C20 H16 O3

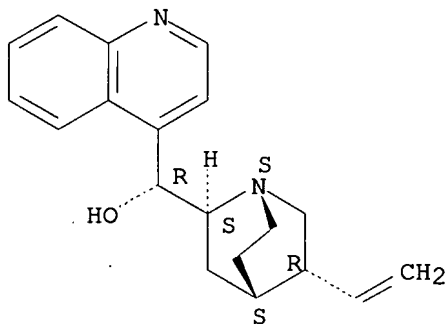


CM 2

CRN 485-71-2

CMF C19 H22 N2 O

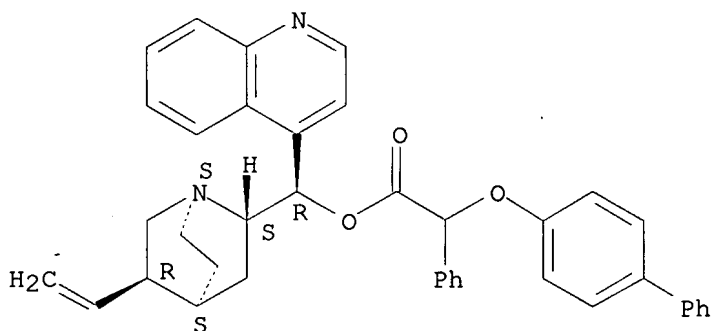
Absolute stereochemistry. Rotation (-).



RN 881738-34-7 CAPLUS

CN Cinchonidine, (4-biphenyloxy)phenylacetate (7CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:93100 CAPLUS

DOCUMENT NUMBER: 64:93100

ORIGINAL REFERENCE NO.: 64:17469e-h,17470a-h,17471a-e

TITLE: Fuerstion. Syntheses of alkyl substituted phthalic acids

AUTHOR(S): Scarpa, J. S.; Ribl, M.; Eugster, C. H.

CORPORATE SOURCE: Univ. Zurich, Switz.

SOURCE: Helvetica Chimica Acta (1966), 49(2), 858-69

CODEN: HCACAV; ISSN: 0018-019X

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 64:93100

GI For diagram(s), see printed CA Issue.

AB cf. CA 47, 5378f. Fuerstion (I), C₂₀H₂₆O₃, isolated from the leaves of East African *Fuerstia africana* is extremely labile to nucleophilic and electrophilic reagents and with the exception of the Cu complex provides no simple functional derivative I. (1.002 g.) added portionwise with shaking to 50 ml. 63% HNO₃ and the mixture refluxed 1 hr. (oil bath, 155°), heated 5 hrs., and distilled (oil bath, 180°), the residue taken up in 10 ml. H₂O and evaporated, the process repeated to cessation of evolution of N-containing gases, the dried residue taken up in alc. and methylated with CH₂N₂, extracted with Et₂O, and the product distilled gave 186-mg. fraction, b_{0.0001} 112-15°, and 402 mg.-fraction, b_{0.0001} 125-35°. The latter fraction treated with a drop of MeOH and kept at 0° gave 58 mg. tetramethyl mellophanate (II), m. 125.0-5.5°. The 1st fraction in 10 ml. EtOH saponified with 2.5 ml. N NaOH and the isolated acid heated with Ac₂O at 130°/0.01 mm., the crystalline fraction recrystd. from Et₂O-petroleum ether, sublimed in vacuo, and recrystd. from tetrahydrofuran and petroleum ether gave the anhydride (III), m. 171-1.5°, of 6,2,3-Me(HO₂C)C₆H₂CH₂CH₂CO₂H (IV). III (10 mg.) boiled in 1 ml. MeOH and methylated with CH₂N₂ in Et₂O gave 6,2,3-Me(MeO₂C)C₆H₂CH₂CH₂CO₂Me, b_{0.01} 120°. The 2nd fraction, freed from II, saponified and the liberated acid converted to the anhydride gave 22 mg. needles of anhydride (V), m. 111.5-12.0°, of 6,2,3-Me(HO₂C)C₆H₂(CH₂)₃CO₂H (Va). Comparison of the uv spectra of substituted phthalic acid anhydrides suggested that III was a Me-substituted phthalic anhydride since N.M.R. detns. and lack of optical activity showed the absence of alkyl branching in the carboxyl-substituted side chain. To decide between the possible formulations, the anhydride of IV, anhydride (VI) of 4,2,3-Me(HO₂C)C₆H₂CH₂CH₂CO₂H, and anhydride (VII) of 2,3,4-Me(HO₂C)C₆H₂CH₂CH₂CO₂H were synthesized. Condensation of 285 mg. Me(CH:CH)CH₂CH₂CO₂H with 199 mg. maleic anhydride in C₆H₆ 14 hrs. gave VIII, m. 185°; Me ester m. 127° (Me₂CO-petroleum ether). VIII (240 mg.) heated 5.5 hrs. at 220-5° (oil bath) with 70 mg. S and the cooled mixture extracted with Me₂CO yielded 45% 3-methyl-6-(2-carboxyethyl)phthalic anhydride (VI), m. 176-7°. H₂C:CHCMe:CHCO₂Et (16.9 g.) in Et₂O reduced at -20° with LiAlH₄ and

the mixture treated with AcOEt and saturated aqueous NH_4Cl , extracted with Et₂O and the washed and dried extract evaporated yielded 90% alc. $\text{H}_2\text{C}:\text{CHCMe}:\text{CHCH}_2\text{OH}$, b_{5.5} 65-6°, converted (4.32 g.) in 60 ml. Et₂O and 1.3 g. $\text{C}_5\text{H}_5\text{N}$ at -10° by addition of 3.95 g. PBr_3 to give the bromide. The bromide (4.5 g.) refluxed 24 hrs. in ligroine (b. 90-130°) with freshly prepared $\text{NaCH}(\text{CO}_2\text{Et})_2$ [from 2.5 g. Na, 5.5 g. alc., 18.6 g. $\text{H}_2\text{C}(\text{CO}_2\text{Et})_2$] gave 3.8 g. $\text{H}_2\text{C}:\text{CHCMe}:\text{CHCH}_2\text{CH}(\text{CO}_2\text{Et})_2$, b_{1.5} 95-7°, saponified with 8% KOH to give the malonic acid, m. 119-21° (PhMe). The acid (204 mg.) and 100 mg. Cu powder heated 35 min. with evolution of CO_2 and the cooled mixture diluted with Et₂O, extracted with NaHCO_3 and the isolated acid distilled gave $\text{H}_2\text{C}:\text{CHCMe}:\text{CHCH}_2\text{CH}_2\text{CO}_2\text{H}$, b₁₁ 120-5°, in 58% yield. Condensation of 91 mg. acid with 64 mg. maleic anhydride in 15 ml. C_6H_6 at 120° 14 hrs. in a bomb tube yielded 87% tetrahydrophthalic anhydride, m. 164-5°, sublimed at 120-5°/0.0001 mm. to provide anal. sample. The anhydride (100 mg.) heated 75 min. at 220° with 26 mg. powdered S and the cooled mass extracted with Me_2CO , distilled at 130-5°/0.0001 mm. and recrystd. from tetrahydrofuran-petroleum ether gave IV, m. 173-3.5°. $\text{H}_2\text{C}:\text{CHCMe}:\text{CHCH}_2\text{CH}_2\text{CO}_2\text{Me}$ treated at 120° in a bomb tube with maleic anhydride in C_6H_6 and the product dehydrogenated 3 hrs. at 220° with S gave IV Me ester, m. 111-12°. $\text{H}_2\text{C}:\text{CHCMe}:\text{CHCO}_2\text{H}$ and N-phenylmaleinimide in PhMe gave the Diels-Alder adduct (IX, R = CO_2H), m. 119-21°, converted to the acid chloride with SOCl_2 and transformed with CH_2N_2 to the diazo ketone IX (R = COCHN_2), m. 148° (decomposition), in 77% yield. Attempts to transform the diazo ketone by a Wolff rearrangement were unsuccessful. Synthesis of VII by Diels-Alder addition of maleic anhydride to 3-(2-methyl-3-furyl)propionic acid (X) was attempted. Reduction of 1.44 g. Me 2-methylfuran-3-carboxylate (XI, R = CO_2Me) in Et₂O with LiAlH_4 and isolation of the product yielded 93% XI (R = CH_2OH), b₁₁ 76-8°. The alc. (1.06 g.) in 60 ml. CCl_4 shaken 8 hrs. with 15 g. MnO_2 at 20° and the mixture shaken 6 hrs. with addnl. 15 g. MnO_2 , the filtered solution evaporated and the residue distilled gave 0.7 g. XI (R = CHO), b₂₂ 70-5°. Treatment of the acid with SOCl_2 in boiling C_6H_6 gave XI (R = COCl), b₁₁ 65-70°, reduced by Rosenmund procedure with 10% Pd-BaSO₄ in xylene in 7-8 hrs. at 120-5° to the aldehyde. The acid chloride treated with CH_2N_2 in Et₂O at -20° and brought to 20° gave XI (R = COCHN_2), m. 61-1.5°. The aldehyde (0.7 g.) and 500 mg. $\text{H}_2\text{C}(\text{CO}_2\text{H})_2$ in 3 ml. $\text{C}_5\text{H}_5\text{N}$ heated 2 hrs. at 110° with addition of a few drops of piperidine and the isolated acid (0.65 g., m. 128-9°) recrystd. from alc.-H₂O and resublimed at 130-5° gave XI (R = $\text{CH}:\text{CHCO}_2\text{H}$) (XII), m. 135-6°. MeOH (5 ml.) containing 200 mg. α-furylacrylic acid treated with 2 ml. $\text{N}_2\text{H}_4\cdot\text{H}_2\text{O}$ and a trace of CuSO_4 , bubbled through 90 min. with 60-70 bubbles of O, separated by acid-base procedure and the product distilled at 70-80°/0.07 mm. yielded 47% 3-(α-furyl)propionic acid (XIII). Similar reduction of XII at 20° in 2.5 hrs. yielded X, b_{0.07} 75-80°. XIII condensed with maleic anhydride in boiling C_6H_6 gave the adduct, m. 97-8°. Attempts at aromatization of the adduct and a similar adduct with X were unsuccessful. The diene, $\text{H}_2\text{C}:\text{CHC}(\text{CH}_2\text{CH}_2\text{CH}_2\text{OEt}):\text{CHR}$ (XIV) (R = Me) (XV) for the synthesis of VII by direct reaction of $\text{H}_2\text{C}:\text{CHCO}(\text{CH}_2)_3\text{OEt}$ with $\text{Ph}_3\text{P}:\text{CHMe}$ could not be realized and a synthesis of XV from $\text{EtO}(\text{CH}_2)_3\text{C}.\text{tplbond}.\text{CH}$ through $\text{H}_2\text{C}:\text{CHC}(\text{OH})(\text{C}.\text{tplbond}.\text{COEt})(\text{CH}_2)_3\text{OEt}$ and XIV (R = CO_2Et , CH_2OH , CH_2Br) was devised. $\text{EtO}(\text{CH}_2)_3\text{C}.\text{tplbond}.\text{CH}$ (36.86 g.) stirred in a closed system (N atmospheric) 16 hrs. in 40 g. H₂O, 20 g. AcOH, and 32 g. 38% HCHO containing 30 g. Et₂NH and 1 g. CuCl at 45° and alkalinized with 10% NaOH, the filtered solution extracted with Et₂O and the product isolated gave 58.6 g. $\text{EtO}(\text{CH}_2)_3\text{C}.\text{tplbond}.\text{CCH}_2\text{NEt}_2$, b₁₅ 123°, hydrolyzed (19.73 g.) by heating 90 min. at 75-80° (N atmospheric) with 100 ml. 10% H₂SO₄ containing 1.5 g. HgSO₄ and the cooled alkalinized

filtrate extracted with Et₂O, the product isolated and distilled over hydroquinone gave 7.8 g. material, b₁₀ 65-80°, freed from amine by shaking with dilute H₂SO₄ and redistn. over hydroquinone to give very unstable H₂C:CHCO(CH₂)₃OEt (XVI). EtMgBr (32 ml. 1.86M in Et₂O) and 70 ml. dry C₆H₆ stirred (N atmospheric) with dropwise addition of 5.12 g. EtOC.tplbond.CH in 50 ml. C₆H₆ at 20° and the mixture heated 2.5 hrs. at 40°, cooled to -15°, and stirred 30 min. with dropwise addition of 8.03 g. XVI in 50 ml. C₆H₆, the mixture stirred 1 hr. at -15° to -5° and 1 hr. without cooling bath, added slowly to 100 ml. aqueous ice-cold 20% NH₄Cl and the product extracted with Et₂O, the extract washed with aqueous NaHCO₃ and the dried extract distilled over hydroquinone gave 8.9 g. XIV (R = CO₂Et), b_{0.005} 53-83°. Reduction of the ester at -20° in Et₂O with LiAlH₄ and working up with 70% MeOH and Et₂O yielded 81% XIV (R = CH₂OH), b_{0.05} 65-80°. The pentadienol (2.24 g.) in 50 ml. Et₂O and 1.05 g. C₅H₅N treated slowly at -15° (N atmospheric) with 2.4 g. PBr₃ in 50 ml. Et₂O and the mixture stirred 4 hrs. at 20°, the filtrate evaporated and distilled at 44-55°/0.02 mm. gave 2.04 g. lachrymatory and extremely moisture-sensitive bromide XIV (R = CH₂Br). LiAlH₄ (80 ml. 0.23M, in Et₂O) diluted with 160 ml. absolute tetrahydrofuran and stirred 15 min. (ice-bath) with dropwise addition of 2.14 g. bromide in 25 ml. Et₂O, the mixture refluxed 2 hrs., and the cooled mixture decomposed with 5 ml. 60% tetrahydrofuran-H₂O, the isolated product filtered through neutral Al₂O₃ in C₆H₆, and the purified material distilled yielded 70% colorless mobile oily XV, b₁₀ 55-60°. XV (970 mg.) and 620 mg. maleic anhydride heated 20 hrs. in 20 ml. C₆H₆ at 90-100° in a bomb tube and the adduct (660 mg.) heated 90 min. at 220-50° (oil bath) with 171 mg. S, the product isolated by CHCl₃-Me₂CO extraction and the extract, filtered through silica gel, distilled at 95-100°/0.0001 mm. and the yellow oil (26%) chromatographed on silica gel, eluted with 4:1 C₆H₆Et₂O and mixts. with increasing Et₂O content and the fraction, λ 222, 262, 302, 311 mμ, redistd. gave the ether (XVI, R = OEt (XVII), m. 35-8°. KI (220 mg.), 55 mg. XVII, and 0.2 ml. 95% H₃PO₄ heated 5 hrs. at 140-5° and the cooled mixture diluted with H₂O, saturated with NaCl, and extracted with Et₂O, the extract washed with aqueous Na₂S₂O₃ and the isolated product crystallized from Et₂O gave 70 mg. XVI (R = I), m. 99-100°. The iodide (31 mg.) in 4 ml. C₆H₆ refluxed 8.5 hrs. with freshly prepared anhydrous AgOAc and the isolated acetate, saponified by stirring 24 hrs. in 10 ml. 2N HCl and some Me₂CO at 110-15° gave 21 mg. XVI (R = OH, as dicarboxylic acid). The product (21 mg.) in 3 ml. AcOH kept 15 hrs. at 20° with 0.13 millimole CrO₃ in 80% AcOH and the mixture heated briefly at 45°, the residue on evaporation taken up in 5% H₂SO₄ and extracted continuously 8 hrs. with Et₂O, the isolated tricarboxylic acid sublimed twice at 120-55°/0.0001 mm. and the sublimate purified by recrystn. from Me₂CO-C₆H₁₄ and sublimation at 130-50°/0.0001 mm. gave 16 mg. anhydride VII, m. 145-7°. XVII (107 mg.) in 6 ml. 35% HNO₃ and a trace of V₂O₅ heated 5 hrs. at 100-10° and the residue on evaporation after repeated addition of H₂O sublimed. The fraction, 135-70°/0.0001 mm., showed the expected uv spectrum and crystallized from Me₂COC₆H₁₄ and tetrahydrofuran-C₆H₁₄ gave a fraction, m. 225°, resublimed to give the anhydride (XVIII). Comparison of phys. data of the anhydride III with those of the synthetic anhydrides III, VI, VII, and XVIII confirmed the structure of IV. With clarification of the structure of IV and Va, 13 of the 20 C atoms of I were accounted for. The γ-substituted butyric acid in Va must result from degradation of a longer side-chain in I or be a rearrangement product.

IT 5555-18-0 5555-19-1 7522-98-7
94465-08-4

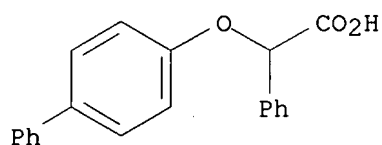
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 5555-18-0 CAPLUS

CN Benzeneacetic acid, α-([1,1'-biphenyl]-4-yloxy)-, (-)- (9CI) (CA

INDEX NAME)

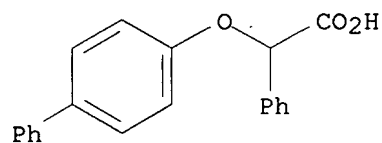
Rotation (-).



RN 5555-19-1 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl-, (±)- (8CI) (CA INDEX NAME)

Rotation (+).



RN 7522-98-7 CAPLUS

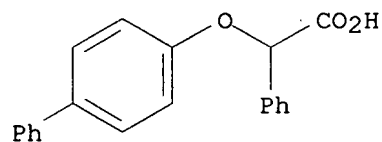
CN Cinchonan-9-ol, (8 α ,9R)-, mono[(-)- α -([1,1'-biphenyl]-4-yloxy)benzeneacetate] (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 5555-18-0

CMF C20 H16 O3

Rotation (-).

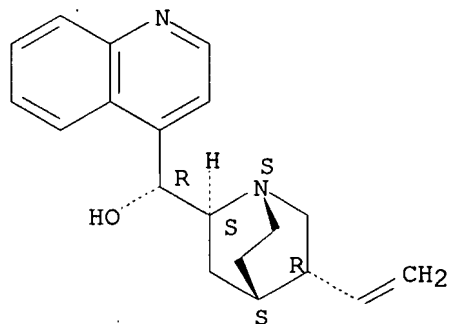


CM 2

CRN 485-71-2

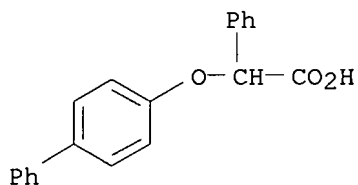
CMF C19 H22 N2 O

Absolute stereochemistry. Rotation (-).

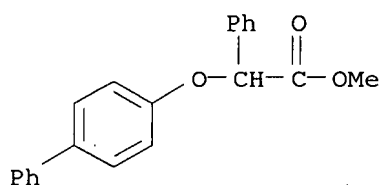


RN 94465-08-4 CAPLUS

CN Acetic acid, (4-biphenyloxy)phenyl- (7CI) (CA INDEX NAME)



IT 5555-10-2P, Acetic acid, (4-biphenyloxy)phenyl-, methyl ester,
(±)-
RL: PREP (Preparation)
(preparation of)
RN 5555-10-2 CAPLUS
CN Benzeneacetic acid, α-([1,1'-biphenyl]-4-yloxy)-, methyl ester (9CI)
(CA INDEX NAME)



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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
122.15	294.46

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-17.94	-17.94

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Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
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L2	0	l1 and tyrosine adj phosphate	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/11/27 12:49
L3	5	l1 and PTP	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/11/27 12:49